MATHEMATICAL METHODS FOR POPULATION GENETICS

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By

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Preface.

Human genetics has been influenced in three main ways, and partly on this account it is possible to distinguish different trends within this science.

Within *anthropology* and *racial research* it has gradually been found necessary to differentiate between heredity and environment. Only properties conditioned by heredity can be racial properties. Racial research has been concerned with working out the reasons why people attain to opulence and a high degree of culture, and then sometimes degenerate and go under. Problems of this kind have given rise to the German designation "race biology", and nowadays a number of authorities have assembled under this title investigations not only dealing with human races but also such as aim at analysing populations in the light of heredity and environment. In so doing, detailed investigations of very different characters have been needed and race biology has gradually come to denote human genetics generally. Actually, however, the term is misleading. It is not a question of working out which race is best; the problem is more general: to find how the inherited characteristics in a people are changed in the one or the other direction. Racial research has, however, added to human genetics a social attitude and an important aspect of the above problem.

Botanical and *zoological genetics* have also proved important influences Mendelism was established and took form within these fields, and has subsequently begun to be applied to investigations on human beings also. Attention was at first primarily paid to rare characteristics; it is, of course, easiest to show that *Mendel*'s laws are applicable to such characteristics. Gradually, however, an immense amount of proof has been collected, and we now have no reason to doubt that *Mendel*'s laws also hold good of the human being. Nowadays, therefore, investigations of this kind are not so important. Rare characteristics are in themselves interesting more as curiosities than from the social viewpoint. To get further, we must try to get some idea of the part heredity plays in more common characteristics.

The application of *statistical methods* to social questions has in a number of cases led to problems touching heredity and environment. The *biometrical* school tried for a long time to solve such problems without using the more special assumptions contained in Mendelism. Gradually, however, the Mendelian attitude has been generally accepted. Human genetics has received important statistical and biometrical contributions in respect of method, acquiring thereby means to investigate the nature of populations from the point of view of heredity.

In human genetics there has gradually grown up a trend aimed at solving problems as to the influence of heredity on characters in *human populations*, taking *Mendelism* as point of departure and using *statistico-mathematical methods*. The investigations made hitherto are comparatively few, however. There is at present no work giving a satisfactory survey of the underlying theoretical questions. This work is intended as a survey of this kind, but it also suggests new solutions to a number of problems. It should perhaps be stated at this point that as this is a first attempt at a synthetic presentation of problems of heredity from the population aspect, it is natural that the presentation should have those deficiencies which are unavoidably linked up with such an attempt.

In this book, the aim of the author has been throughout to make it comprehensible to persons with no mathematical training. In order for the reader to accustom himself in successive steps to the methods of calculation used here, the presentation has been given a very elementary form, especially in the first part of the book, which to mathematically trained readers must seem irritating and tedious. This does not necessarily mean that a number of other readers may not find the book difficult to read. (In this case, the reader may perhaps be recommended to resort to the old method of reading the last chapter first, in order to stimulate interest.) It has in any case been possible to complete the presentation by using elementary mathematical methods. The difficulties in this sphere lie not so much in the mathematical calculations as in grasping the ideas and outlining the problems.

Human genetics has on the whole gone too far in imitating the methods and problems pertaining to experimental genetics. The author hopes that this work will bring about a different view of human genetics, and also arouse interest in some problems of social importance. It has naturally been particularly difficult to take into account the literature in this field, partly on account of the times, partly because works touching on the problems treated here are scattered in journals of very different types. The references to literature given are therefore without doubt incomplete. A German edition of this book was published as supplement No. 148 to Acta Medica Scandinavica, 1943. I believed at the time that the Germans would especially need sensible information on the subject after the war. In the English edition now published very few alterations have been made. I have warmly to thank Professor Leslie Dunn for reading the first part of the book and Doctor D. J. Finney for reading the last part of it.

Contents.

Division of characteristics from a hereditary viewpoint.

Strictly speaking, all characteristics in living organisms are determined by hereditary tendencies, genes, and also, at the same time, by environment. The genes in a fertilized egg must have a certain nature for the egg to be able to develop for a longer or shorter period. The constitution of the genes can, however, vary within certain limits. If the constitution of the genes deviates too much from the average of the species, the fertilized egg cannot develop, or will only do so for a short time. The environment, too, can only vary within certain limits if there is to be development. If the environment diverges too much from what is normal for the species, there can be no development. Genes and environment, then, can vary within the limits set by death. The characteristics of an individual are therefore always determined both by genes and environment. Naturally, the state of an individual at a given moment is also dependent on his age. A certain characteristic is therefore, strictly speaking, always determined by 1. hereditary factors, 2. environmental factors, and 3. an age factor.

When assessing an individual's characteristics, we often try to eliminate the age factor by comparing individuals of the same age. In a number of presentations of the problem, this factor is left out of account. Particularly in problems of heredity and environment is the age factor often tacitly disregarded, a proceeding naturally justified if this factor is of no importance for the special characteristic or characteristics in question, or if the argument postulates a comparison between individuals of a certain definite age. Generally the constitution of the individuals in adulthood, before increasing age has become noticeable, is discussed. It is not possible to say exactly how long this period is. We assume, however, that the limits are drawn to be on the safe side. During this period we have certainly right to consider the importance of the age factor to be little or nothing in most of the cases. Yet this is by no means always the case, in particular with regard to disease. When in the following chapters the age factor is in general passed over in the theoretical argument, this implies a conscious simplification. When solving a specific practical problem this must be kept in mind.

In a given case particular investigation must, if necessary, determine the part played by this factor.

We must assume, then, that a certain characteristic in an individual is always determined by both environmental and hereditary factors. Which group of factors is to be assigned the greatest importance depends on their respective frequencies. Assume that a characteristic is determined by a hereditary factor and an environmental factor. If both the hereditary and the environmental factor is present in all individuals, the characteristics will always be there. This, then, is of no interest from the point of view of genetics. Characteristics present in all individuals are considered of interest only in discussions of differences between human beings and closedly allied animal species, but they are, of course, of no importance when the problems bear on differences between human beings. If the environmental factor is always present and the hereditary factor present in a part of the population, but not in all individuals, this means that those individuals without that hereditary factor have another such factor. The population falls into two groups, between which there is a difference determined by heredity. If, on the other hand, the hereditary factor is found in all individuals but the environmental factor only in a group of the population, there is a difference determined by environment between the two population groups. If a population shows two hereditary factors and two environmental factors, which have a different distribution, the appearance of the characteristics must be determined by a coincidence of hereditary and environmental factors. There is a difference between two groups, conditioned by the fact that in one group a hereditary and an environmental factor have coincided, whereas in the other group only the hereditary factor is present, or only the environmental factor, or neither. In the latter case, the characteristics are absent. (It is of course possible that there are differences of characteristics between the three last-mentioned groups, also.) On these theoretical starting-points, we thus arrive at the following classification.

The first group consists of *hereditarily determined characteristics in the proper sense.* These characteristics are but little affected by environment. They depend upon a certain combination of genes for their existence. If this combination is there, the characteristic is always present in the individual, no matter how the environment varies. If the environment diverges unduly from the normal, both characteristic and individual cease to exist. In other words, the characteristic has little or no

variability conditioned by the environment; or, expressed otherwise, the necessary environmental factors are always present. Now as, in practice, one as a rule never knows how individuals with this combination of genes react to all conceivable environmental factors, it is clear that the statement that a characteristic in the actual sense is hereditarily conditioned can only claim a certain limited validity. It is conceivable that some rare and untested environmental factor might change the way in which the combination of genes manifests itself. When we pronounce a characteristic in the proper sense to be hereditary, we refer, then, only to the more usual environmental factors, "normal" for the species.

The second group consists of characteristics whose existence is in the first place *determined by one or more not unduly common environmental factors*. The genes necessary for the environmental factors in question to produce the characteristics exist in practically speaking all individuals in the species or population investigated. The environmental factors in question affect only some of the individuals in the population. Under such conditions it will be the environmental factors that play the deciding part. An example of this is typhus. Practically speaking, everyone has the hereditary constitution that disposes them to fall ill if infected with typhus germs. We say, therefore, that the disease is determined by the occurence of the infection; strictly speaking, however, a certain hereditary constitution is necessary here, too. Dogs, for example, are immune to typhus. If a dog is infected by typhus germs, he does not contract the disease; his hereditary make-up is different from that of man. Thus certain genes are necessary for the existence of these environmentally determined characteristics, too, but when the genes are commonly present, they do not play the deciding part in any one case.

The third group comprises characteristics *determined by a coincidence of environmental and hereditary factors*, which are neither of them always present in the individuals in the population. The hereditary factors occasion a certain *disposition*, a leaning to react in a certain way to definite environmental factors. Individuals lacking this disposition do not react at all, or very little, to the special environmental factors; whether these exist or not is of very little consequence to them. Individuals with the disposition determined by special genes react to the special environmental factors in a different way, on the other hand. Such characters may be termed *constellationally* determined.

In all groups the question may be one of characteristics which can be found in *healthy individuals*, and which do not make for any limitation of fitness for life, and such as make for a more or less reduced adaptation to the demands of life. If the reduced adaptability is very moderate, so small that the individual is inconvenienced by the characteristic more by way of exception, we speak of *anomalies*. If, on the other hand, the reduction is greater, we speak of *disease*.

In any case, it is clear that in all the groups the characteristics may be of either more incidental or more permanent nature. A hereditary characteristic is, of course, fairly independent of environment, and if it is of a more incidental nature, this merely means that it is present for a short time at a certain age. Particularly striking is the accidental nature of hereditary diseases, which rapidly lead to death. There are many examples of accidental characteristics among those determined by environment; among these may be reckoned a number of infectious diseases, such as typhus, measles, etc. More permanent characteristics determined by environment include a number of diseases, e.g. syphilis, and the immunity consequent on certain accidental, environmentally determined diseases, e.g. measles. The group of constellational characteristics shows a special need for a division in respect of the accidental or permanent nature of the characteristic. The accidental constellational characteristics include a large number of infectious diseases, susceptibility to which hardly seems to be general in human populations, e.g. encephalitis lethargica and poliomyelitis. A constellational characteristic of a more permanent nature is, for example, a disease like tuberculosis, which postulates a certain disposition, certain genes, and an environmental factor, tuberculosis infection, and which results in a characteristic which in many cases has a fairly permanent nature.

As the last example shows, the limit between our different groups is by no means sharp. It is to a certain extent a matter of taste whether a characteristic be regarded accidental or permanent, as also whether a certain combination of genes is so usual that its reaction to more infrequent environmental factors shall be thought to make for characteristics possible to denote as determined by environment. It is also clear that when genes of this kind react to some more usual environmental factor in one way, and to another more unusual factor in another, it is also to a certain extent a matter of taste whether the one or the other characteristic is to be considered abnormal or normal respectively.

As regards environmental factors, we can also discuss whether such a factor is common enough to enable us to put the main stress on the hereditary factor. If we assume that general paralysis is, at bottom, due to a special way of reacting, determined by heredity, we can also say that the disease is conditioned by environment in so far as only those infected with syphilis are affected with paralysis. In a population where syphilis is very widespread, so that nearly everyone becomes infected, we would, however, have reason to consider the disease determined by heredity.

Summing up, it may be suggested that, in classifying characteristics, the frequency of the hereditary and environmental factors which play a part thus comes to be of great importance for the designation of the characteristic. If the hereditary and the environmental factor alike are of importance for the genesis of the characteristic, and both kinds of factors occur with moderate frequency, the characteristic is termed constellational. If the environmental factor is very usual and is present in almost the entire population, the characteristic is termed hereditary in the proper sense of the word. If, on the other hand, the hereditary genes have a very high frequency and the environmental factors a low one, the characteristic is taken to be determined by environment. If both hereditary and environmental factors occur in the whole of the population, then all individuals possess the characteristic and there are no hereditary differences in the population; if the hereditary and environmental factors disappear, then the characteristic disappears from the population.

The system proposed and the limits we have set are therefore to a certain extent arbitrary. The classification used here of characteristics from the point of view of heredity and environment has only recently been presented by the author (*Dahlberg*, 1939 a), and is therefore not universally accepted. Whether the system and the terminology based on this system is practicable remains to be seen. For the present, however, the system should suffice to clarify the rôle of heredity and the importance of the environment, and to give a more differentiated grasp of these problems.

The conception of race and the laws of Mendel.

As was stated in the preface, human genetics has acquired impetus from racial research, and obtained a fundamental presentation of the problems from this quarter. We are therefore justified in seeking to analyse in more detail the conception of race from a Mendelian point of view.

The designation "race" is used, and questions of race are discussed, in an unclear way. Definitions of the conception of race are usually content with stating that a race is a group of individuals differing in respect of hereditarily determined characteristics from other groups. This definition may at first sight seem clear and unequivocal, but as a matter of fact it is in many respects extremely vague.

The conception of race is older than Mendelism, and this has meant that its elaboration has been based on views of heredity existing before *Mendel*. These older views were never clearly defined, or at all clearly thought out; they have, nevertheless, gone on being used long after the advent of Mendelism, though to a certain extent simultaneously with the ideas of this last. The result of this has been that the word "race" has come to cover very obscure and elastic conceptions.

Actually, the definition given above must in its turn be defined more exactly in three respects.

We must first and foremost be clear as to what is meant by a *characteristic determined by heredity*. This question has already been discussed here, and it appears from the analysis which has been made that we cannot only differentiate between hereditary and environmental characteristics. Obviously, constellational characteristics can be racial characteristics in the extent to which hereditary factors affect such characteristics.

This side of the matter is of less importance, however. A more important side is that racial research, as has already been stated, proceeds from pre-Mendelian ideas as to the nature of inheritance. When analysing the nature of matter, there are two assumptions to choose from. We can assume that matter is constructed of homogeneous substances which may have different natures and which may mix in different ways.

The scientists worked for a long time with this conception of matter. Only when it was assumed that matter was made up of small parts, molecules, atoms, etc., that could not be split up without being destroyed, was it possible to reach an agreement between the experimental results and the theoretical ideas. There are the same alternatives to choose from as regards the nature of the inherited mass. Before *Mendel* it was assumed that this mass was a substance. Among the pure races, this substance had a certain constitution, and matings between different races made for mixed races in the same way as mixtures of different metals give alloys of different character. If a negro and a white man are crossed the result should be a hybrid race, a mulatto. If mulattoes are crossed, the offspring should be mulattoes, for the same reason as the mixture of two portions of an alloy gives the same alloy as before. The fact that the offspring of mulattoes vary does not agree with what one would theoretically expect.

Mendelism implies an important step forward, since it made theory and empiricism agree. As we know *Mendel* assumed the inherited mass to consist of small parts, genes, which could combine in different ways.

The pre-Mendelian view is still used to a certain extent in racial research, however. It is assumed that pure races have existed. The constitution of the race is taken to be of very great importance in the appraisal of separate individuals. The individuals can, it is true, display differences, but those of the same race are, in essentials, nevertheless alike. The argument is illustrated by saying that certain metals may also have a different constitution and be kitchen utensils or ornaments, but must all the same be considered, in essentials, to be similar. Both the assumption of originally pure races and that which ascribes fundamental importance to the racial constitution are incorrect.

The individuals of a race vary very greatly. Two persons have never quite the same genotype. Individuals who can be relegated to different races in respect of derivation may be far more like one another as regards important genes than those belonging to the same race. Two normally gifted individuals belonging to different races are in crucial matters more alike than a normally gifted person and a genetical idiot who belong to the same race. Two races may show hereditarily determined differences as regards certain genes, so that the genes are absent in the one and present in the other. The differences may, however, be relative, and only mean that certain genes have a different frequency in the two races.

To be able to determine the racial difference beyond all doubt we would need to know the nature of the genes in every individual in the two groups we wish to compare. Our knowledge at present is extremely patchy, so that the statements that might be made about racial constitutions must have a very limited value. However, there are without doubt distinct differences between different groups of individuals. These differences must have a name. We are therefore justified in speaking of racial differences. It must always be remembered, however, that statements can only be made about certain investigated characteristics, and that we cannot construct from what we know further differences about which we know nothing. It may seem unnecessary to say this, but the very fact of dealing with pre-Mendelian views means there is always a strong temptation to let our actual knowledge over-reach itself. If a difference has been established between two chemical substances, there is reason to suspect further differences. In the same way, if a difference is established between two groups on pre-Mendelian postulates, it is tempting to assume further differences, and this stimulates speculations leading to an over-estimation of the importance of the racial differences.

It is also necessary to go into what may be meant by a *group of individuals*, when defining the conception of race. We do not jump to the conclusion that the tall persons in a nation belong to one race and the shorter to another, although both can be said to form groups, and both display differences conditioned by heredity. This is because individuals of different height have for many generations intermarried. Actually, when talking of a group in connexion with race, we mean a group of persons who for a very long time have been mated mainly with each other, and not at all or to a lesser extent with the other group compared with it. In actual fact the group is to constitute an isolate (or a number of isolates), which are either geographically or socially limited.

Finally, the definition says that the two groups must display different characteristics. We then ask how many characteristics are required to enable us to speak of a particular race. The smallest difference possible refers to a single characteristic; thus, theoretically, we only need to establish one difference concerning a characteristic to be justified in speaking of a particular race. (Cf. *Dahlberg*, 1941.) Under such circumstances, we thus get the following definition:

A race is an isolate or a group of isolates consisting of individuals displaying at least one hereditary absolute or relative difference from other isolates.

In other words, a characteristic is a racial characteristic if it occurs in an isolate or a group of isolates, but is missing or occurs with another frequency in some other isolate. Strictly speaking we should talk not of racial characteristics but of racial differences. It is furthermore clear that the racial differences may have very different orders of magnitude, and it is therefore desirable to get a gauge for them. This question will be dealt with further on, for before this it is necessary to discuss in more detail the mechanisms which may set up differences in the genetic constitution in a people.

Different forms of inheritance.

Monohybrid diallelism.

If there is only one kind of gene in a pair of allelomorphs all the individuals in a population will be homozygotes and of the same genetic constitution. In a population of this kind, the differences between the individuals are determined solely by a variability occasioned by the environment. In monohybrid diallelism, the characteristics in question are, on the other hand, determined by two different genes (diallelism), belonging to an allelomorphic pair (monohybridity). Let us call these genes *R* and *D*. The *gametes* which are formed may be of two kinds: those containing *R* genes and those containing *D* genes. When the gametes unite as *zygotes*, they form three kinds: zygotes resulting from the union of *R* gametes, which thus contain two *R* genes and are called homozygous for the *R* gene, those containing two *D* genes, called homozygous for the *D* gene, and those produced from the union of *R* gametes and *D* gametes, called heterozygotes. As regards the characteristics corresponding to this hereditary composition of the zygotes, we have different possibilities. 1. One gene may *dominate* over the others. If the *D* gene is dominant, the heterozygotes resemble the homozygotes for the *D* gene in characteristics. It is impossible to see that the respective individuals have a different hereditary make-up; only by demonstrating with mating experiments or the like that the heterozygotes produce two different kinds of gametes can it be established that they are not identical as to composition with the homozygotes for the *D* gene. If the *D* gene dominates, the *R* gene is said to be *recessive*. In this case, then, we get two different kinds of characteristics. 2. The heterozygotes may occupy an intermediate position between the homozygotes. If the homozygotes for the *R* gene are white and those for the *D* gene are black, the heterozygotes in such a case will be gray. We then speak of *intermediate* inheritance. 3. The heterozygotes may be quite different from the homozygotes. Let us assume that the *R* homozygotes are white and the *D* homo-

zygotes black. If in this case the heterozygotes are red in colour, that is to say quite different from both kinds and outside the range of variation that can be thought to connect the two kinds of homozygotes, we speak of *extramediate* inheritance (the term is previously used by *Gunnar Dahlberg*, 1942 a; *Johannsen*, 1926, speaks in this case of "heterozygotic constructions", a term which may easily prove misleading). There is, of course, no hard and fast line between intermediate and extramediate inheritance.

Sex-linked monohybrid diallelism.

In this form of inheritance, males have only one of the two possible genes. Thus, we have two different kinds of males: those with an *R* gene, agreeing in characteristics with homozygotes for the *R* gene (which latter appears only in females), and those with a *D* gene, agreeing in characteristics with homozygotes for the *D* gene (which are likewise only found in females). So that we have only two different kinds of male both as regards genes and characteristics. In females, on the other hand, the genes occur in allelomorphic pairs, giving the different possibilities in genes and characteristics as we described above in monohybrid diallelism. A recessive gene only present in the Y chromosome cannot have any effect. If the gene is dominant, the characteristics are found only in males and are inherited only by sons. The females are not conductors. This theoretically conceivable mechanism of inheritance has not been observed, however, with human beings.

Monohybrid polyallelism.

There are three different kinds of genes in monohybrid *triallelism*, of which, however, only two at most can be present at the same time in a zygote. The characteristics investigated are determined, therefore, by a pair of allelomorphs (monohybridity) and by genes of three different kinds (triallelism). Let us assume that the genes in question are *D*, *R*, and *I*. Since only one of the genes can be present in one gamete, we get three different kinds of gamete corresponding to these different kinds of gene. Since only two gametes can unite into one zygote, we get three different kinds of homozygotes, namely *DD*, *RR*, and *II*. Further we have three kinds of heterozygotes: *DR*, *RI*, and *DI*. As regards the characteristics in these different kinds of individual, we have different possibilities. The homozygotes may each have a dif-

ferent characteristic, the heterozygotes may be intermediate or extramediate. Finally, there may also be a question of dominance here. The possibility most readily presenting itself is that one gene dominates over the two others, thus *D* over *R* and *D* over *I*, and that the second gene is dominant over the third, e.g. *R* over *I*. In this case we get three different kinds of character-bearers: *DD*, *DR*, and *DI* individuals, all of whom have the same characteristic, *RR* and *RI* individuals, who have another characteristic, and finally *II* individuals, who have a third characteristic. Another possibility is that two of the genes each dominate over the third, but that the heterozygotes with these two dominant genes have intermediary or extramediary composition. In this latter case we say that there is simple dominance, whereas in the former case, when one gene dominates over the other two, we say that there is double dominance.

Now, of course, an unlimited number of genes, of which only two are present at the same time, is conceivable. We group all cases where there are more than two different kinds of genes under the title of monohybrid polyallelism. To clarify the possibilities in monohybrid polyallelism, we assume we are dealing with an arbitrary number of genes which we will call *n*. This being so, we can get *n* different kinds of gametes. With the help of the combination rules we can calculate how many different kinds of zygotes can be formed through combination of these different kinds of gametes. In this case we have a series of elements (gametes) of *n* different kinds. We take two elements from this series and make them into a pair; the question then is: how many different kinds of pairs can we make? In the first place we can combine every gamete carrying a certain kind of gene with itself. This gives us homozygotes, and these have the same number of kinds as the gametes, i.e. *n*. We get the heterozygotes by making two groups of the different elements, without, however, taking their order into account; it is of no consequence whether gene No. 1 is combined with gene No. 2 or gene No. 2 with gene No. 1. In this case, then, we get according to the rules given above, $\frac{n\,(n-1)}{1 \cdot 2}$ different kinds of heterozygotes. Thus in monohybrid polyallelism where there are *n* different genes and therefore *n* different gametes, we get altogether $n + \frac{n\,(n-1)}{2}$ individuals of different hereditary composition. The process

	G_1	G_2	G_3	G_4	G_5
G_1	$G_1 G_1$	$G_1 G_2$	$G_1 G_3$	$G_1 G_4$	$G_1 G_5$
G_2	$G_2 G_1$	$G_2 G_2$	$G_2 G_3$	$G_2 G_4$	$G_2 G_5$
G_3	$G_3 G_1$	$G_3 G_2$	$G_3 G_3$	$G_3 G_4$	$G_3 G_5$
G_4	$G_4 G_1$	$G_4 G_2$	$G_4 G_3$	$G_4 G_4$	$G_4 G_5$
G_5	$G_5 G_1$	$G_5 G_2$	$G_5 G_3$	$G_5 G_4$	$G_5 G_5$

Fig. 1. Cf. the text.

is shown graphically in Fig. 1. The different kinds of gametes (genes) in question are entered along the two sides of a square. Let us call the gametes G_1, G_2, G_3, G_4, and G_5; the scheme then covers the formation of zygotes in monohybrid quintallelism. The homozygotes are obtained by entering in the diagonal squares the designations vertically and horizontally above the squares at the sides. The heterozygotes are obtained by the same procedure with the squares above (or below) the diagonal ones. The squares below will contain the same designations (though in inverted order) as those above.

As regards the constitution of these individuals, we have to take into account different combinations of simple or manifold dominance, and intermediate or extramediate inheritance.

Sex-linked monohybrid polyallelism.

In this form of inheritance the same conditions prevail for the females as were previously described for monohybrid polyallelism. The males, on the other hand, have only one of the different kinds of gene in question. If this number is n, we thus get n kinds of hereditarily differing individuals, all of whom also have different characteristics. If, then, sex-linked monohybrid polyallelism (or diallelism) manifests more different kinds of characteristics among females than among men, we can assume that the females with no equivalents in the men are heterozygotes.

Polyhybrid diallelism.

There are two pairs of allelomorphs in dihybrid diallelism, and the two genes in each pair are different. Let us assume that the one pair is made up of the genes D_1 and R_1 and the other of the genes D_2 and R_2.

When the gametes are formed, only one of the genes in each pair will be included. We now combine the D_1 gene with each of the two genes in the other pair, and get D_1D_2 and D_1R_2 gametes. We then combine the R_1 gene with each of those in the other pair and get the gametes R_1D_2 and R_1R_2. This means four different kinds of gamete, which can be calculated by multiplying D_1+R_1 by D_2+R_2. Thus:

$$(D_1+R_1)\cdot(D_2+R_2) = D_1D_2+D_1R_2+R_1D_2+R_1R_2.$$

	D_1	R_1
D_2	D_1D_2	R_1D_2
R_2	D_1R_2	R_1R_2

Fig. 2. Cf. the text.

Fig. 2 shows the process diagramatically. The pairs of genes are written along the horizontal and the vertical sides of a square respectively. The square is divided into four, and the composition of the gametes is obtained in each quarter by entering the respective horizontal and vertical designations.

As the gametes combine with one another to form zygotes, the same argument and formula as in monohybrid polyallelism can be used. In this case we are dealing with four different kinds of gametes, four different elements, which combine at random to form pairs. To start with, similar elements can unite, and since we have four different kinds of element, we get four different kinds of homozygotes. The heterozygotes are found by the formula $\frac{n\,(n-1)}{2}$. In this case $n=4$. Thus we get six different kinds of heterozygotes. The diagram for the process is similar to that in monohybrid polyallelism.

	D_1D_2	D_1R_2	R_1D_2	R_1R_2
D_1D_2	$D_1D_1D_2D_2$	$D_1D_1D_2R_2$	$D_1R_1D_2D_2$	$D_1R_1D_2R_2$
D_1R_2	$D_1D_1D_2R_2$	$D_1D_1R_2R_2$	$D_1R_1D_2R_2$	$D_1R_1R_2R_2$
R_1D_2	$D_1R_1D_2D_2$	$D_1R_1D_2R_2$	$R_1R_1D_2D_2$	$R_1R_1D_2R_2$
R_1R_2	$D_1R_1D_2R_2$	$D_1R_1R_2R_2$	$R_1R_1D_2R_2$	$R_1R_1R_2R_2$

Fig. 3. Cf. the text.

We write the different kinds of gamete along the sides of a square (Fig. 3), which is divided into smaller squares. By transferring to the *diagonal* squares the gamete constructions from the vertical and horizontal outer rows, we obtain the homozygotes. By filling in the small squares *above* (or below) these diagonal squares, we get the heterozygotes. It is plain that the squares above and below the diagonal will have the same composition.

The different possibilities for the zygotes are obtained mathematically by multiplying the following expressions by each other:

$$(D_1D_2+D_1R_2+R_1D_2+R_1R_2) \cdot (D_1D_2+D_1R_2+R_1D_2+R_1R_2).$$

The coefficients are of no interest in this connexion, so that in this case we get four different kinds of homozygotes and six different kinds of heterozygotes, in all ten different kinds.

It is of course conceivable that intermediate or extramediate inheritance, prevailing throughout, is in question. In this case we also get ten different kinds of characteristic. Another possibility is simple dominance: then the one gene dominates over the other in each pair, while on the other hand neither gene from one pair is dominant over one in the other. This gives us four different kinds of characteristic. Finally there is the possibility that the one dominant gene dominates over the other, and then we get only three different characteristic bearers.

We finally want to know the result if we are dealing with a larger number of gene pairs combining with one another. Let us assume m pairs of allelomorph genes; we then get $2m$ different kinds of gene. We assume, then, that the different pairs have the following composition:

$$D_1 R_1;\ D_2 R_2;\ D_3 R_3;\ \ldots D_m R_m.$$

The gametes are formed by the union of one gene from each pair with one of the genes from all the others. Mathematically, the kinds of gamete are elicited from this expression:

$$(D_1+R_1) \cdot (D_2+R_2) \cdot (D_3+R_3) \ldots (D_m+R_m).$$

The number of different kinds of gamete is thus 2^m.

When the gametes combine with one another, we have in the first place to take into account the possibility of different kinds of gamete uniting with one another to form homozygotes. We have 2^m different

kinds of gamete, and therefore get 2^m different kinds of homozygotes. In the formation of the heterozygotes we combine as usual 2^m gametes with each other regardless of the order between the gametes in the pairs obtained. We thus get

$$\frac{2^m(2^m-1)}{2}.$$

As regards the nature of the characteristics in these individuals this situation naturally also provides a large number of possible combinations between different kinds of dominant and intermediate or extramediate inheritance.

Sex-linked polyhybrid diallelism.

In sex-linked polyhybrid diallelism we have as usual as many hereditarily different kinds of individual and different kinds of characteristic-bearers as we have gametes—i.e. in this case, using the previous designations, 2^m men different in respect of hereditary constitution and characteristic. For the females, the conditions are as in polyhybrid diallelism. As regards intermediate or extramediate inheritance, therefore, the different kinds of characteristic bearers are more numerous in females than in men.

Polyhybrid polyallelism.

In theory, of course, there is also the possibility of an arbitrary number of allel pairs, one or more of which may have an arbitrary number of genes, of which, however, only two can be present at the same time. Clearly, this is an extremely complicated situation, all the more so as, on the appearance of the characteristics, we must also take into account different kinds of dominance, intermediate and extramediate inheritance. It can hardly be of any interest to go into these different possibilities in more detail; we have only drawn attention to the matter for the sake of completeness.

Composition of populations in panmixia.

When investigating heredity in human populations, it is assumed in the first place that the marriages in the population are contracted at random, as it were, and that different groups of characteristic-bearers propagate themselves to the same extent. In a population where this is the case, panmixia is said to obtain. In many cases this assumption undoubtedly holds with sufficient accuracy.

But panmixia is not always present, of course. Deviations from the results which would be obtained in random mating, panmixia, can be caused only in five ways (cf. *Dahlberg*, 1941).

1. One cause of deviation from the composition in panmixia is *selection*. The hereditarily different kinds of individuals in a population may be varyingly fertile, so that sharp progressive displacements in the composition of a population are set up from generation to generation. As, in point of fact, the generations overlap one another and are not sharply delimited, this makes for a population composition diverging continuously from panmixia.

2. *Consanguineous marriages* increase the probability of homozygosis. The assumption of panmixia involves the further assumption that relatives, too, will marry at random. The degree of homozygosis thus occasioned is therefore included in the results calculated on the assumption of panmixia. If, however, there is inmarriage to a greater or a lesser extent than that which we would expect in panmixia, this naturally occasions a divergent composition of the population.

3. If individuals marry at random, they nevertheless do so only within a certain limited area and among a certain number of individuals. Obviously, an individual belonging to a certain social class and a certain geographical area has the chance of marriage only with a limited number of individuals in the population of the country. From this point of view a larger population falls into part populations, which we call *isolates*. These are separated off by geographical and social isolate limits. Panmixia can be assumed to obtain within these isolates. If they differ from one another in constitution, a lumping together of the isolates to form a population gives another composition of the total

material than would be obtained if panmixia obtained throughout the population.

4. Deviations from panmixia can be occasioned by *assortative mating*, which term implies the marriage of character-bearers to a greater (or less) extent than that determined by coincidence. The process makes for an increase (or decrease) of the homozygous frequency in a population.

5. *Mutations* may, theoretically, alter the hereditary constitution of a population from one generation to another, and thus give it a composition deviating from that expected in panmixia.

Variants of the different mechanisms for deviations from panmixia fall under these main headings. Theoretically, it should be possible to relegate every deviation to one of them. In many cases panmixia may undoubtedly be assumed. The composition of the population then remains constant, and the proportion of the genes does not change from one generation to another, as the different genes are propagated to the same extent. If, however, formulas constructed on the assumption of panmixia are to be employed in any one case, it is of course necessary to see that this assumption really does hold with a satisfactory degree of accuracy.

Composition of a population in monohybrid diallelism.

If we want to calculate the composition of a population in respect of a monohybrid diallelous character in panmixia, an appropriate starting-point is the nature of the gametes in the population. Let us assume that, among the gametes produced by the individuals, the recessive gene R occurs with a frequency of r, and the dominant gene D with a frequency of d. The probability of picking at random a gamete with the recessive gene is consequently r, and d for one with the dominant gene. As these two probabilities exclude one another, their total is 1. Thus

$$r+d = 1$$

and

$$r = 1—d.$$

Now, when the individuals producing these gametes marry one another this means a certain limitation of the gametes' freedom of

movement. In any one marriage, zygotes can be produced only through union of the kinds of gametes the married pair produced. Monogamy thus means a certain limitation in the gametes' random freedom of movement. For our purposes, however, this limitation is of no consequence, as shown by *Dahlberg*, 1926. We can imagine all the gametes produced by the individuals in the population as constituting a single mass and collected in a lake, where they meet by chance. In reality, the mechanism is more complicated, but it gives the same results as the simple process described above. Let us, then, assume that the gametes meet by chance; the probabilities for the combinations then arising can be easily calculated, since we know the probability for the different kinds of gamete.

When the probability for an R gamete is r, an R gamete will have the probability $r \cdot r = r^2$ of meeting with another R gamete to form a zygote with the composition RR.

When the probability for a D gamete is d, a D gamete will have the probability $d \cdot d = d^2$ of meeting with another D gamete to form a zygote with the composition DD.

And, finally, the probability for a meeting between an R gamete and a D gamete to form a zygote with the composition RD (or DR) is $2rd$.

Therefore:

The probability for recessive homozygotes (RR), i. e. recessive character bearers, is . . . r^2.

The probability for heterozygotes (RD) is . . . $2rd$.

The probability for dominant homozygotes (DD) is . . . d^2.

Thus the probability for the production of dominant character-bearers ($RD+DD$) is $= 2rd+d^2 = 1 - r^2$
and further, since $r+d = 1$,

$$r^2 + 2rd + d^2 = 1. \qquad (1)$$

Now we know that the homozygotes produce only R or D gametes respectively, whereas the heterozygotes produce half of each. Assuming, therefore, that the rate of propagation is the same for all the individuals, the proportion of gametes in those they produce must be obtained from the number of recessive homozygotes + half the number of heterozygotes. The same holds for the D gametes. Thus

$$r = r^2 + rd$$

and

$$d = d^2 + rd.$$

If then, the number of recessive character-bearers (and hence the number of dominant bearers also) is known in a population of a certain size, r and d can easily be calculated from the expression above. With the help of the values obtained for r and d, the number of heterozygotes in the population can be computed[1]).

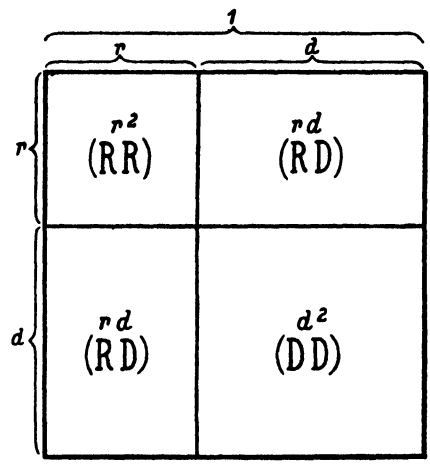


Fig. 4. Diagram showing the types of zygotes in a population (RR, RD and DD) when the gene proportion r:d = 2:3. (After Dahlberg-Hultkrantz, 1927.)

The composition of a population according to these equations is illustrated in Fig. 4. In this figure the side of the square is divided in the proportion $r:d$ (in this case 2:3). The size of the field r^2, of the two fields rd, and of the field d^2 shows the frequency of the different kinds of individuals (*RR*, *RD*, and *DD* individuals) in a population with this gene content. The field r^2, that is to say, corresponds to the recessive character-bearers, and the other fields together to the dominant character-bearers.

[1]) It was *Hardy* (1908) who first suggested the use of formulæ for the composition of a population in panmixia, also showing that in panmixia the nature of heredity of the population remains constant. This was already previously pointed out by *Pearson* (1903) for the ratios 1 : 2 : 1.

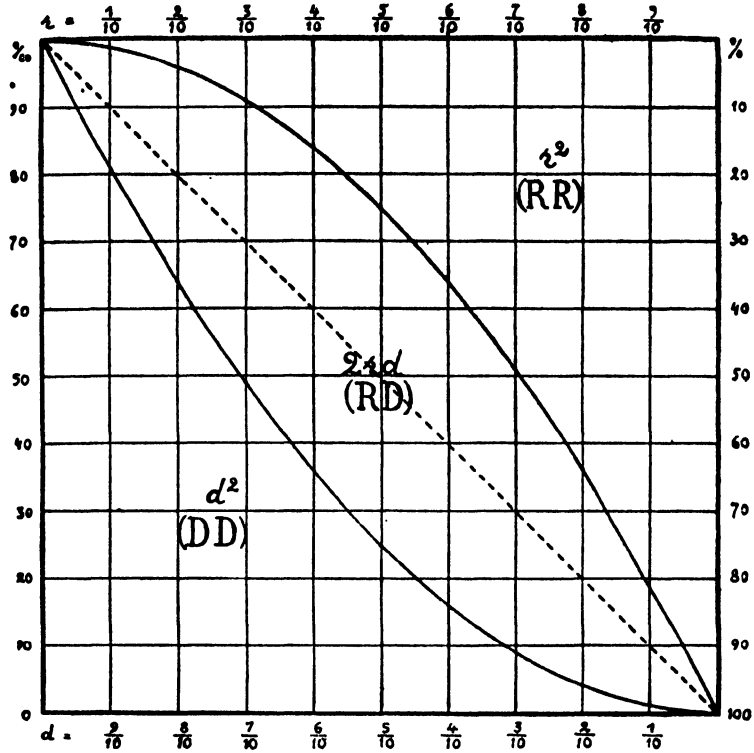


Fig. 5. Diagram showing the types of zygotes in a population with increasing gene proportion (broken line). The numerical values are read off in vertical direction. (After Dahlberg-Hultkrantz, 1927.)

The diagram, Fig. 5, shows the composition obtained in panmixia with different gene proportion in the population. The broken diagonal gives the different possible proportions of *R* and *D* gametes (from $\frac{0}{1}$ to $\frac{1}{0}$; *r* above, *d* below the line). The vertical distance between the fulldrawn curves gives the corresponding percentage of heterozygotes. The distance from the curves to the upper and lower limit of the square respectively gives the percentage of dominant and recessive kinds of homozygotes respectively. The ordinates for the upper curve give the percentage of dominant character-bearers.

In Fig. 6 the full-drawn curve indicates the percentage at different frequencies for recessive and dominant character-bearers, whose percentages are found under the abscissa. The broken symmetrical curve

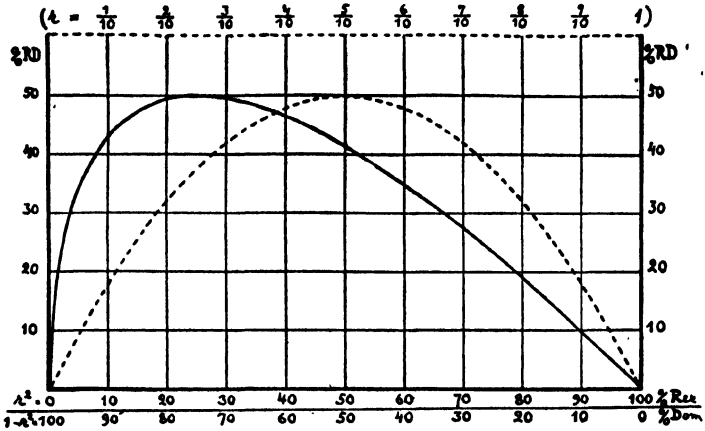


Fig. 6. Percentage figures of heterozygotes with different proportion of recessive and dominant character-bearers (whole line; the figures below) and with different proportion of recessive genes (broken line; the figures above). (After Dahlberg-Hultkrantz, 1927.)

in the same figure indicates also the percentage of heterozygotes, but in relation to the proportion of R genes (r) given in the figure. Table 1 gives exact figures for a number of possible population compositions in monohybrid diallelism.

It appears from the diagrams and the table that the heterozygotes can at most constitute 50% of a population, and that this maximum is reached when R and D genes are equally common, i. e. each has the probability of $\frac{1}{2}$, the recessive homozygotes thus comprising $\frac{1}{4}$. In this case the composition of the population will be characterized by the classical Mendelian numbers: $\frac{1}{4} : \frac{1}{2} : \frac{1}{4}$. The greater the difference becomes between the frequencies for the R and the D genes, the less will be the frequency of the heterozygotes compared with the population in its entirety.

The equations drawn up above are thus of interest for one thing because they make it possible to calculate the number of the heterozygotes in monohybrid diallelous recessive-dominant inheritance (and naturally, in intermediate or extramediate inheritance also). As in this form of inheritance the heterozygotes agree in appearance with the dominant homozygotes, they cannot be directly observed and assessed.

TABLE 1. Percentage of heterozyg. with different gene proportions in a population. 23

RR zygotes 100 r^2	RD zygotes 100 2rd	DD zygotes 100 d^2	RR zygotes 100 r^2	RD zygotes 100 2 rd	DD zygotes 100 d^2
0.01	1.98	98.01	45	44.16	10.84
0.05	4.37	95.58	46	43.65	10.35
0.1	6.12	93.78	47	43.11	9.89
0.2	8.54	91.26	48	42.56	9.44
0.3	10.35	89.35	49	42	9
0.4	11.85	87.75	50	41.42	8.58
0.5	13.14	86.36	51	40.83	8.17
0.6	14.29	85.11	52	40.22	7.78
0.7	15.33	83.97	53	39.60	7.40
0.8	16.29	82.91	54	38.97	7.03
0.9	17.17	81.93	55	38.32	6.68
			56	37.67	6.33
1	18	81	57	37	6
2	24.28	73.72	58	36.32	5.68
3	28.64	68.36	59	35.62	5.38
4	32	64	60	34.92	5.08
5	34.72	60.28	61	34.20	4.80
6	36.99	57.01	62	33.48	4.52
7	38.92	54.08	63	32.75	4.25
8	40.57	51.43	64	32	4
9	42	49	65	31.25	3.75
10	43.25	46.75	66	30.48	3.52
11	44.33	44.67	67	29.71	3.29
12	45.28	42.72	68	28.92	3.08
13	46.11	40.89	69	28.13	2.87
14	46.83	39.17	70	27.33	2.67
15	47.46	37.54	71	26.52	2.48
16	48	36	72	25.71	2.29
17	48.46	34.54	73	24.88	2.12
18	48.85	33.15	74	24.05	1.95
19	49.18	31.82	75	23.21	1.79
20	49.44	30.56	76	22.36	1.64
21	49.65	29.35	77	21.5	1.5
22	49.81	28.19	78	20.64	1.36
23	49.92	27.08	79	19.76	1.24
24	49.98	26.02	80	18.89	1.11
25	50	25	81	18	1
26	49.98	24.02	82	17.11	0.89
27	49.92	23.08	83	16.21	0.79
28	49.83	22.17	84	15.30	0.70
29	49.70	21.30	85	14.39	0.61
30	49.54	20.46	86	13.47	0.53
31	49.36	19.64	87	12.55	0.45
32	49.14	18.86	88	11.62	0.38
33	48.89	18.11	89	10.68	0.32
34	48.62	17.38	90	9.74	0.26
35	48.32	16.68	91	8.79	0.21
36	48	16	92	7.83	0.17
37	47.66	15.34	93	6.87	0.13
38	47.29	14.71	94	5.91	0.09
39	46.90	14.10	95	4.94	0.06
40	46.49	13.51	96	3.96	0.04
41	46.06	12.94	97	2.98	0.02
42	45.61	12.39	98	1.99	0.01
43	45.15	11.85	99	0.9975	0.0025
44	44.66	11.34	100	0	0

It is of particular interest to examine the relation of the heterozygotes to that of recessive and dominant homozygotes respectively. With the aid of the expressions drawn up above, we find that:

$$\frac{\text{Heterozygotes}}{\text{Recessive character-bearers}} = \frac{2rd}{r^2} = \frac{2\,(1-r)}{r}, \tag{2}$$

$$\frac{\text{Heterozygotes}}{\text{Dominant character-bearers}} = \frac{2rd}{d^2+2rd} = \frac{2r}{1+r}. \tag{3}$$

Now, if we look first at the equation for the relation between heterozygotes and recessive character-bearers, we find that if r is a small number, approaching 0, the relation between them approaches ∞. If r is a small fraction the frequency of the recessive character-bearers (r^2) will be extremely small. If, then, the recessive character-bearers are very rare in a population, there will be relatively many heterozygotes or latent character-bearers. From the point of view of the population both the latent and the manifest bearers are rare, the latter, however, incomparably more so than the former.

This also applies to the relation of the heterozygotes to the dominant homozygotes. If a rare character is in question, the main part of the bearers are heterozygotes. Conversely, in questions of a very common dominant gene (approaching 1), the heterozygotes constitute a dwindling fraction of the dominant bearers.

These conclusions as to the relation of the heterozygotes to the homozygotes have a certain importance for the methods of genetics. If, for example, we start from the character-bearers and examine their brothers and sisters, we get a different composition of these latter circles in different frequencies of one gene. In theory, it is possible to calculate from the constitution of such groups the frequency of the genes in the relevant population—provided the mode of inheritance is known (cf. *Dahlberg-Hultkrantz*, 1927). In practice, however, it would hardly be possible to reach reliable frequency figures along these lines. In theory, again, it is possible to compute from the hereditary constitution of dichorial twins the frequency of genes in the population from which the pair was taken. *Rife* (1938) has drawn up equations for calculations of this kind, also reproduced in *Dahlberg* (1942 b). In the latter work the designations used in this book have been used.

Composition of a population in sex-linked monohybrid diallelism.

In sex-linked monohybrid diallelism the characteristic in question is determined by one gene only in the males, and by a pair of genes in the females. The males produce germ cells either with no gene at all having anything to do with the character in question, or containing one gene; both these two kinds of cell are produced to the same extent, i. e. each have a probability of $\frac{1}{2}$. The females produce only cells with one gene. In fertilization there arise either individuals with only one gene with the character in question and which are always of the male sex, or individuals with two genes for the characters, which are always female. Thus, the males constitute two kinds of sperms, and the sex of an individual is determined by the nature of the sperm fertilizing the ovum whence he or she developed.

Mathematically, the simplest problem is offered by the populational composition in sex-linked monohybrid diallelism in the case of man.

Let us assume as before that the composition of the population is to be calculated in respect of a recessive gene R with the frequency r, and a dominant gene D with the frequency d. In women we then get the same conditions as in monohybrid diallelism, i. e. recessive character-bearers or RR individuals with the probability r^2 and dominant heterozygotes with the probability $2rd$, and also dominant homozygotes with the probability d^2. As regards the other conditions, we refer to what has been said above on monohybrid diallelism.

As far as the males are concerned, the state of affairs is even more simple. The different kinds of character-bearer have the same frequency as the different kinds of gene. Thus we get individuals with the recessive character in r cases and those with the dominant character in d cases. Since the two genes can never be present in the same male, the one gene in the males can never dominate over the other. Thus, the designation recessive and dominant character-bearer is improperly used as regards males; however, the individuals with R genes, whom we consequently call recessive character-bearers, will agree in respect of the characters with the recessive bearers in females.

Now follows a particularly interesting fact: if the frequency of the recessive character-bearers in males is known, then the square of their probability among the males gives the probability for these characters among the females; conversely, if we know their probability among

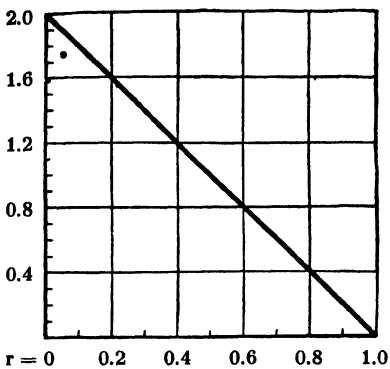
the females, we can get from its square root their probability among the males. According to our equations the relation between recessive character-bearers among the males and the females respectively is:

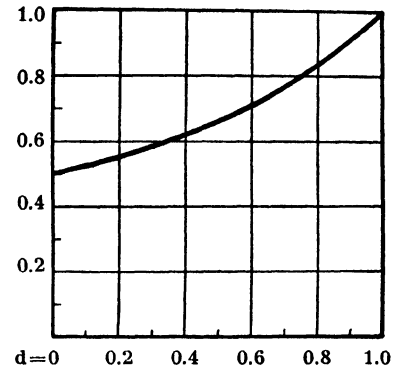
$$\frac{\text{"recessive" character-bearers among males}}{\text{recessive character-bearers among females}} = \frac{r}{r^2} = \frac{1}{r}.$$

We can illustrate this by an example. An investigation of colour blindness in boys and girls gave the following figures (*Waaler*, 1927): Among boys, 1 % protanopia, 1 % protanomaly, 1 % deuteranopia, 5 % deuteranomaly: i. e. 8 % in all. We would then expect to find among the girls 0.01 % protanopia, 0.01 % protanomaly, 0.01 % deuteranopia, and 0.25 % deuteranomaly, i. e. a total of 0.28 %. The theoretical figures have been obtained according to the equation given by squaring the frequency figures for the boys. The observed figure for the girls is 0.44 ± 0.07 %; thus the expected and the observed figures agree to within 3 times the standard error. (It should also be taken into account that the observed figures for boys have a standard error which affects the calculated ones.)

The equation we used is interesting from another point of view, too. The ratio of male recessive character-bearers to female is $1:r$. Now, if r is a very small number, i. e. if male character-bearers are extremely rare in the population in question, they will even so be infinitely more common than the female ones; these latter will therefore be still rarer than the male ones. If we assume, for example, that male character-bearers are present in 1:1,000 individuals, female character-bearers will be present in 1:1,000,000.

Another relation, also interesting, is that between female carriers and male character-bearers. This relation is expressed by $2rd:r$, which when simplified gives $2(1-r):1$. This expression shows that if the male character-bearers are rare (r approaches 0), the female carriers will double their number. In a more common character, the preponderance is less. If the recessive character is present in half the male population, the female bearers will constitute an equally large number. If it is even commoner, the relative number of bearers among the women will sink even more. The relation is illustrated by the accompanying diagram (Fig. 7).





Figs. 7 and 8. Cf. the text.

The relation between male character-bearers and the female dominant character-bearers is determined by the expression $\frac{d}{d^2 + 2rd}$, which simplified gives $\frac{1}{2 - d}$. This expression shows that if a gene is rare in a population (d approaches 0), there will be nearly half as many male as female dominant character-bearers in the population. If the gene is more common, the female character-bearers preponderate less. If the male bearers constitute half of the male population, the female bearers will make up $\frac{3}{2}$ of the male—i. e. $\frac{3}{4}$ of the female part of the population. Finally, if the gene is extremely common (d approaches 1), male and female character-bearers will constitute practically the whole of the population and be about equally common. The relation is illustrated in the accompanying diagram (Fig. 8).

A postulate we have used above all the time is that men and women each constitute one half of the population. Actually, this postulate only holds approximately. The proportion of the sexes deviates somewhat in that the boys preponderate slightly among the new-born. The proportion is subsequently displaced so that in higher age-goups the relative number of the boys gets less and less until their ratio is finally reversed, giving a preponderance of women. The deviation from the assumed sex proportion is, however, so small that it can hardly affect the problems we are concerned with here. If, on the other hand, more exact calculations are desired in any one case, there is of course nothing to prevent a modification of the above equations in respect of a sex proportion differing from the one assumed here.

The composition of a population in panmixia and monohybrid triallelism.

In monohybrid triallelism the genes determining the characters in question here occur in pairs, formed from the three different kinds present in the population. According to a previous calculation (p. 12) this would give us six different kinds of individuals, namely, three different kinds of homozygotes and heterozygotes respectively. Let us assume that we have an R gene with the probability of r in the population, a D gene with the probability d, and an I gene with the probability i. Thus, $r+d+i = 1$. We then get the following different kinds of individuals in the following frequencies:

RR individuals with the probability ..... r^2,	who have the character 0 and the frequency p in the population.
DR individuals with the probability ..... $2rd$	who have the character A and the frequency q in the population.
DD individuals with the probability ..... d^2	
RI individuals with the probability ..... $2ri$	who have the character B and the frequency s in the population.
II individuals with the probability ..... i^2	
DI individuals with the probability ..... $2di$,	who have the character AB and the frequency $1-p-q-s$.

Above, we have assumed two dominant and one recessive gene, and also that individuals possessing the two dominant genes deviate in appearance from the two kinds possessing only one dominant gene. This is of course by no means the only possibility: one gene may be recessive, another dominant over it, and a third dominant over both. However, we will now take the first possibility, assuming in addition that the different character-bearers have the frequency in the population that we assumed above in the scheme. We then get the following equations:

$$r^2 = p,$$

$$2rd+d^2 = q,$$

$$2ri+i^2 = s,$$

$$2di = 1-p-q-s.$$

From these equations we get:

$$r = \sqrt{p}, \tag{4}$$

and by inserting this value in the second and third equation we get:

$$d = \sqrt{p+q} - \sqrt{p}, \tag{5}$$

$$i = \sqrt{p+s} - \sqrt{p}. \tag{6}$$

We know besides that:

$$r+d+i = 1. \tag{7}$$

As we now know the value of d and i, we can calculate the frequency of the group AB, which according to our scheme is $2di$. This gives the equation: $s = 1+p+q+2\sqrt{p}-2\sqrt{p+q}-2\sqrt{p\,(p+q)}$. By comparing this total with the frequency of this group found empirically, we can check whether a population consisting of four different kinds of character-bearers in given frequencies can conceivably have arisen from monohybrid triallelism. We get another check from the equation $r+d+i = 1$. If there is inheritance according to this mechanism, the total values of the gene frequencies calculated from the equations should give 1.

In monohybrid triallelism we also have to take into account the possibility, already mentioned, that one of the three genes, R, with the frequency r, is recessive, one gene, D_2, with frequency d_2, dominates over both the first and the second gene, which we call D_1 with frequency d_1. This then gives us three different kinds of character-bearer in the population. We then get the following different individuals with their frequencies:

RR individuals with probability	r^2,	who have the character 0 and the frequency p.
D_1R individuals with probability	$2rd_1$	who have the character A and the frequency q.
D_1D_1 individuals with probability	d_1^2	
D_2R individuals with probability	$2rd_2$	who have the character B and the frequency $1-p-q$.
D_2D_2 individuals with probability	d_2^2	
D_1D_2 individuals with probability	$2d_1d_2$	

With the help of these expressions we get the following equations:

$$r^2 = p,$$

$$2rd_1 + d_1^2 = q,$$

$$2rd_2 + d_2^2 + 2d_1d_2 = 1 - p - q.$$

We know that:

$$r + d_1 + d_2 = 1. \tag{8}$$

These equations give:

$$r = \sqrt{p}, \tag{9}$$

and by inserting this value in the second equation:

$$d_1 = \sqrt{p+q} - \sqrt{p}, \tag{10}$$

and by insertion in the third equation:

$$d_2 = 1 - \sqrt{p+q}, \tag{11}$$

and this is the only check we can make in this case.

Thus, if we have three different types of character-bearer in a population, our first interest will be to see whether the frequency of the types agrees with the assumption of monohybrid diallelism with intermediate heredity. From the frequencies of the individuals assumed to be homozygotes, we calculate the frequency of the respective genes; the sum of these frequencies should be 1. From these frequencies can further be computed the frequency of the heterozygotes. On both these points (agreement between calculated and observed heterozygote frequency and the fact that the sum of the gene frequencies shall be 1) we can now check whether the composition of the population agrees within the limits of the standard error with this assumption. Should this not be the case, we can suspect monohybrid triallelism with double dominance. To check this, we calculate the frequency of the three genes: their sum should be 1. Any other result argues against monohybrid triallelism with double dominance.

If, on the other hand, there is agreement, it nevertheless does not indicate monohybrid triallelism with double dominance and monohybrid diallelism with intermediate heredity respectively. A more complicated course of heredity may be in question, which none the

less sometimes gives the required agreement with the simpler mechanism. A more definite proof can only be obtained from an analysis of the relations of the character-bearers.

The composition of a population in dihybrid diallelism.

In dihybrid diallelism the characters in question are determined by two pairs of genes. In the first we assume that the gene R_1 has the probability r_1, and the gene D_1 the probability d_1. In the other pair we assume that R_2 has the probability r_2, and D_2 the probability d_2. The genes can now combine to form the following types:

$R_1R_1R_2R_2$ with the frequency	$r_1^2r_2^2$,	which have the character 0 and the frequency p in the population.
$R_1R_1R_2D_2$ with the frequency	$2r_1^2r_2d_2$	which have the character A and the frequency q in the population.
$R_1R_1D_2D_2$ with the frequency	$r_1^2d_2^2$	
$R_1D_1R_2R_2$ with the frequency	$2r_1d_1r_2^2$	which have the character B and the frequency s in the population.
$D_1D_1R_2R_2$ with the frequency	$d_1^2r_2^2$	
$R_1D_1R_2D_2$ with the frequency	$4r_1d_1r_2d_2$	which have the character AB and the frequency $1-p-q-s$ in the population.
$R_1D_1D_2D_2$ with the frequency	$2r_1d_1d_2^2$	
$D_1D_1R_2D_2$ with the frequency	$2d_1^2r_2d_2$	
$D_1D_1D_2D_2$ with the frequency	$d_1^2d_2^2$	

Above we have assumed two gene pairs, each composed of one recessive and one dominant gene; further that when the two dominant genes are present at the same time, one in no wise dominates over the other, but gives instead a character or complex of characters deviating from those conditioned by a sole dominant gene in heterozygous or homozygous form. If we take the frequency of the different character-bearers in the population according to the scheme above, we get the following equations in the derivation of which we use the expression $r_1+d_1=1$, $r_2+d_2=1$, and consequently $d_1=1-r_1$, $d_2=1-r_2$:

$$r_1^2 \cdot r_2^2 = p,$$
$$r_1^2(1-r_2^2) = q,$$
$$r_2^2(1-r_1^2) = s,$$
$$(1-r_1^2)\ (1-r_2^2) = 1-p-q-s.$$

From the first three equations we find that:

$$p = (p+q)\ (p+s).$$

The solution with regard to r_1, r_2, etc. gives:

$$r_1 = \sqrt{\frac{p}{s+p}} = \sqrt{p+q}, \tag{12}$$

and:

$$r_2 = \sqrt{\frac{p}{q+p}} = \sqrt{p+s}, \tag{13}$$

and also:

$$d_1 = 1 - \sqrt{\frac{p}{s+p}}, \tag{14}$$

and:

$$d_2 = 1 - \sqrt{\frac{p}{q+p}}. \tag{15}$$

As well as this we know that:

$$p\,(1-p-q-s) = r_1^2\,(1-r_2^2)\,r_2^2\,(1-r_1^2) = qs, \tag{16}$$

and:

$$\begin{aligned}(q+1-p-q-s)\,(s+1-p-q-s) &= \left[r_1^2\,(1-r_2^2) + \right.\\ &+ \left.(1-r_1^2)\,(1-r_2^2)\right]\left[r_2^2\,(1-r_1^2) + (1-r_1^2)\,(1-r_2^2)\right] =\\ &= (1-r_2^2)\left[r_1^2 + (1-r_1^2)\right](1-r_1^2)\left[r_2^2 + (1-r_2^2)\right] =\\ &= (1-r_2^2)\,(1-r_1^2) = 1-p-q-s. \end{aligned} \tag{17}$$

The last *conditional equations* give a possible check of the values of r_1, d_1 and r_2, and d_2, which are calculated from the previous equations.

We have described above the composition of a population in dihybrid diallelism with two dominant genes, neither of which dominates over the other. We must also take into account the possibility of double dominance, however, i. e. where we have two recessive and two dominant genes, but where the one dominant gene is epistatic over the others. We then get only three different kinds of character-bearer according to the following table, where we assume that the gene d_1 dominates over all the other genes.

$R_1R_1R_2R_2$ with the frequency	$r_1^2r_2^2$,	which have the character 0 and the frequency p in the population.
$R_1R_1R_2D_2$ with the frequency	$2r_1^2r_2d_2$	which have the character A and the frequency q in the population.
$R_1R_1D_2D_2$ with the frequency	$r_1^2d_2^2$	

$R_1D_1R_2R_2$ with the frequency $2r_1d_1r_2^2$
$D_1D_1R_2R_2$ with the frequency $d_1^2r_2^2$
$R_1D_1R_2D_2$ with the frequency $4r_1d_1r_2d_2$
$R_1D_1D_2D_2$ with the frequency $2r_1d_1d_2^2$
$D_1D_1R_2D_2$ with the frequency $2d_1^2r_2d_2$
$D_1D_1D_2D_2$ with the frequency $d_1^2d_2^2$

which have the character B and the frequency $1-p-q$ in the population.

If we take the frequency in the population of the different character-bearers from the above scheme, we get the following equations. We know that $r_1+d_1 = 1$, and consequently $d_1 = 1-r_1$; also $r_2+d_2 = 1$ and consequently $d_2 = 1-r_2$.

$$r_1^2 \cdot r_2^2 = \mathrm{p},$$

$$r_1^2 (1-r_2^2) = \mathrm{q},$$

$$r_2^2 (1-r_1^2)+(1-r_1^2) (1-r_2^2) = 1-r_1^2 = 1-\mathrm{p}-\mathrm{q},$$

which gives:

$$r_1 = \sqrt{p+q}, \tag{18}$$

and:

$$r_2 = \sqrt{\frac{\mathrm{p}}{p+q}}, \tag{19}$$

and also:

$$d_1 = 1-\sqrt{p+q}, \tag{20}$$

and:

$$d_2 = 1-\sqrt{\frac{\mathrm{p}}{p+q}}. \tag{21}$$

The composition of a population in polymeric diallelism.

In this form of heredity we have a larger or smaller number of allelomorphic gene pairs, each gene having the same effect as the others; consequently any gene is replaceable by any other one without this causing any noticeable difference as regards the composition of the individual's characters.

Let us assume that we have the gene pairs D_1R_1; D_2R_2; D_3R_3; ... $D_m R_m$, which genes have the frequency d_1r_1; d_2r_2; d_3r_3; ... $d_m r_m$. If the genes combine at random to form gametes, we get the combinations arising from the equation:

$$(d_1+r_1) \cdot (d_2+r_2) \cdot (d_3+r_3) \ldots (d_m+r_m).$$

If the gametes are then assumed to unite at random with one another, we get the frequency of the zygote combinations by multiplying the above expression by itself. The different zygote combinations will thus have the frequencies produced by the following expression:

$$[(d_1 + r_1) \cdot (d_2 + r_2) \cdot (d_3 + r_3) \ldots (d_m + r_m)]^2.$$

If we now assume that the different genes all have precisely the same effect, a zygote with only R genes will have base composition, whereas a zygote with one D gene and the rest R genes can be said to diverge by one unit from the basic composition, a zygote with two D genes can be said to diverge two units, and so on. Let us further assume that all D genes are equally common (the frequency $= d$) and all R genes also have the same frequency ($= r$). This would then simplify the above expression to:

$$(r + d)^{2m}.$$

If $r = d = \frac{1}{2}$, i. e. R and D genes are equally common, we then get a binomial distribution. Individuals with only R genes will be comparatively rare, as also those with only D genes. Between these two extremes we get a so-called binomial distribution, which when the number of characters is great approaches the distribution of the "probability" equation. Characters determined by an inheritance mechanism of this kind should, then, give a distribution agreeing fairly closely with a normal curve. The aspect of the distribution otherwise depends first and foremost on whether the characters are strictly hereditary, unaffected by environment, or whether environment causes a greater or lesser variability. In the first case we will get a distribution with the classes sharply marked off. We get a polygon, agreeing with some one binomial distribution, and can then compute how many polymeric genes we have from the number of sharply demarcated classes. If, for example, there are three gene pairs in question, we get the following frequency for the seven different classes: 1:6:15:20:15:6:1.

This special case is probably so rare, however, that it is hardly to be realized. In the first place, the environment usually has some small effect on the characters in question here. This effect may be expected to be distributed according to a probability equation over every her-

editarily different class of character-bearer. The population will then show a distribution according to a probability function made up of several probability distributions. A curve thus constituted cannot as a rule be analysed before quite a number of arbitrary assumptions have been made. A number of criteria for such a distribution can nevertheless be obtained from a closer analysis of the hereditary data as gathered from families and relations.

Already in this latter case, however, our starting-points have been very much schematized. It is hardly likely that the *R* and the *D* genes are equally common. If the *D* genes are commoner and a smaller number of polymerics is in question, we must expect a more or less skew distribution. If, on the other hand, there is a large number of genes, or the genes in the different pairs have frequencies with an opposite trend (i. e. in one allelomorphic pair the *D* gene is commoner than the *R* gene, in another, the *R* gene is commoner than the *D* gene) the skewness will get less and perhaps disappear. We have assumed that *D* genes dominate over *R* genes. It is naturally also possible to reckon with intermediate inheritance, i. e. that *RD* individuals of a certain pair of genes occupy a middle position between *RR* and *DD* individuals.

Summing up, then we can say that in polymeric polyhybrid diallelism we are likely to get a distribution agreeing more or less well with a probability curve, but which may show a more or less marked skewness. It is, of course, also conceivable that the distribution shows a curtosis possibly due to the modifying effect of the environmental factors. If the effect of the factors varies in strength, the excess may also be attributed to hereditary factors.

For the rest, it may be said that the same result is to be expected in questions of polymeric polyallelism. It is hardly necessary to go into the lines of thought here in more detail, since they are analogous to those on which our present argument is based.

As an example of characters which may be assumed to have a hereditary mechanism of this kind, we can take the stature of man. Anthropological investigations have shown that the stature in a population displays a distribution agreeing fairly well with a normal curve. Most of the materials also show a slight skewness, and sometimes, an unimportant curtosis. It is at once clear that the variability depends in part on environmental factors. It is shown, however, that most of it derives from hereditary factors. When, despite this, there

is a distribution of this kind it must be due to the hereditary factors also causing a distribution according to a normal curve; this indicates with fairly great certainty a polymeric hereditary mechanism." At present, however, it is impossible more closely to analyse the problem and establish how many hereditary factors are in question, how great an effect each one has, and with what frequency the respective genes are represented in a given population.

The composition of a population in more complicated forms of heredity.

In the previous pages we have worked out the composition of a population in monohybrid diallelism, sex-linked monohybrid diallelism, monohybrid triallelism, dihybrid diallelism and polymeric diallelism. Taking the calculation methods used here as model, it should not be very difficult to draw up equations for more complicated forms of heredity. It would hardly be worth while to draw up general formulæ for the different forms of heredity conceivable; we may remember that we have to reckon with an infinite number of possibilities. Firstly, there may be an arbitrary number of allelomorphic genes (polyhybridism). Secondly, an arbitrary number of genes go to make the different pairs, but only two genes are contained in any *one* pair (polyallelism). Thirdly, we must take into account, in respect of the nature of the character, the possibility of simple or varying degrees of manifold dominance, and further, that of intermediate or extramediate inheritance. Lastly, there is the possibility of sex-linked inheritance to be considered.

If we know the number of character-bearers of different kinds in a population, it is possible with the formulæ found above or with those made for the purpose to reach—at any rate in a number of cases—the simplest genetical pattern, agreeing with the frequency of the character-bearers. For all that, it is not proved that there is not a more complicated mechanism in reality. Certain figures agree as well with a simpler inheritance formula for the population as they do with a more complicated one. Under such circumstances it is, of course, most correct to try with investigations of family groups and relations to reach an idea of the inheritance mechanism in a given case, and then try to verify the results by a comparison with the conditions in

the population as a whole—provided that material is available. The fact is, however, that for most of the characters, there are no population statistics, so that such a comparison is only possible by way of exception. This is a further reason why we have not thought it worth while to go in more detail into the different possible population compositions from the point of view of heredity. Nevertheless, the comparatively brief and incomplete account given above has brought us to certain general principles both interesting in themselves and also helpful when drawing up formulæ used in human genetics. For a better appraisal of these conclusions, however, it is necessary to work out in more detail how far the primary postulate of panmixia can be said to hold with adequate accuracy.

The effect of mutations on the composition of a population in panmixia.

We know from zoological and botanical genetics that mutations very rarely appear in various organisms. We know little about them in man, however. We have no exact idea of their frequency, but we do know that they have been very rarely observed or the data would not be so scanty. *Haldane* (1935) has tried to calculate the approximate mutation frequency for certain characters, and obtained the figure 10^{-5}. The mere fact that the mutations must be so rare means that their importance for the composition of the population must, in so much as a short view is taken, be very small. If we compare the composition of the population now and one or several generations ago, we can at once assume that possible mutations are so infrequent that they cannot set up any noticeable difference between the two. But this does not mean that the mutations are of no consequence when investigating how a population develops over a very long period. Although they are rare it is not out of the question that they then cause quite distinct changes.

Let us take a population with panmixia, and assume that the mutations are primarily in the form of heterozygotes with the mutative gene R. We also assume that the frequency of the mutations among the genes during one generation is μ; further, that the mutated individuals have as much chance of propagating themselves as the others, and that no mutations take place among the mutated genes. If the generation we start with is taken as the first, in the n^{th} generation the mutated genes will have a frequency among the total genes according to the following formula:

$$1-(1-\mu)^n, \tag{22}$$

and the non-mutated genes will have the frequency

$$(1-\mu)^n. \tag{23}$$

On the assumption that μ is a very small number, the frequency of the mutated genes will be very nearly expressed thus:

$$1 - e^{-\mu n}, \tag{24}$$

and the non-mutated genes thus:

$$e^{-\mu n}, \tag{25}$$

where, as before, n is the number of generations and μ the mutation frequency per generation.

The formula shows that if the mutation frequency approaches 0 the gene composition of the population will not at first be noticeably changed. Only after a long time does the effect begin to be noticeable, and after an infinite number of generations all genes will have mutated. But in reality we do not have infinite spaces of time to reckon with. Furthermore, mutated individuals in whom the gene manifests itself often have not the same chances of propagation as those lacking the character determined by the mutated gene. In a number of cases the new character-bearers have greater chances of propagation, and then the change proceeds more rapidly than appears from the formulæ above. In other cases the new character-bearers have less chance of propagation, and then the process is slower, or stops at a state of balance, or else the mutation dies out. As has been indicated above, problems of this kind are extremely interesting when explaining the genesis of new species, though as regards man they are less important. Our possibilities of forecasting the future are very limited, so that it can hardly be of interest to try and discuss what will have come to pass after a considerable number of generations. It may be remembered that if we set so-called historical time at 6,000 years, and reckon each generation as covering 25 years, this time corresponds to 240 generations. For a fly, in whose world there is a new generation every month, this would correspond to 20 years. We shall be touching on the question of the mutations' importance in the discussion on the effect of selection in man.

The effect of selection on a population.

Total negative selection.

There may be many reasons why individuals with a certain hereditary composition have fertility below the average of the population. The hereditary composition may be such that they die before reaching sexual maturity, that they become sterile, or that their marriage value is particularly low. Sterilizing measures or other steps taken for eugenic reasons may stop individuals of a certain hereditary type from propagation, etc.

To illustrate the effect of selection in principle we will assume that all character-bearers of a certain type are entirely prevented from propagation (total selection); we shall furthermore assume monohybrid diallelism.

It then becomes immediately clear that if the *dominant* character-bearers are prevented from propagating themselves, the gene will at once be eradicated. There is no doubt that this is why there are, practically speaking, no very serious hereditary diseases which appear regularly before sexual maturity, and which are inherited as a dominant. Such character-bearers practically never get as far as propagation, and are therefore unable to pass their gene on to any offspring. A practical example of this is juvenile amaurotic idiocy. Children suffering from this hereditary disease begin to change at age 6—8 and to exhibit dulled intelligence and a gradual onset of blindness. The process is such that they die before becoming adult. If this character were inherited as a monohybrid dominant one, it would disappear from the population after a generation. But it cannot be inherited thus, as character-bearers occur, albeit in a low frequency.

The situation is quite different for the *recessive* character-bearers. Let us assume that we have an R gene with the frequency r. The recessive character-bearers, RR individuals, will therefore have the frequency r^2. These latter are then prevented from propagating. The gametes giving rise to the next generation will be decreased by this number and their frequency will thus be $1-r^2$; among these $r-r^2$ are

R gametes. In the next generation, the frequency of R gametes (r_2) will therefore be the following:

$$r_2 = \frac{r - r^2}{1 - r^2} = \frac{r}{1 + r}.$$

As a result, the frequency of RR individuals in the next generation will be:

$$r_2^2 = \left(\frac{r}{1 + r}\right)^2.$$

These character-bearers are again prevented from propagating, and the next generation will thus be produced by the following number of gametes:

$$1 - \left(\frac{r}{1 + r}\right)^2.$$

Among these, the following number are R gametes:

$$\frac{r}{1 + r} - \left(\frac{r}{1 + r}\right)^2.$$

Thus we find that in the third generation the frequency of R gametes (r_3) is:

$$r_3 = \frac{r}{1 + 2r}$$

and, finally, in the n^{th} generation their frequency is:

$$r_n = \frac{r}{1 + (n - 1)\, r}.$$

It is easy to show that if the formula holds for n generations, it also holds for $n + 1$ generations.

If we now use this formula to calculate the composition of the zygotes in a population after n generations, we get the following:

Frequency of recessive character-bearers *RR*:

$$r_n^2 = \frac{r^2}{[1 + (n-1) \cdot r]^2}. \qquad (26)$$

Frequency of heterozygotes *RD*:

$$2 r_n d_n = \frac{2r[1 + (n-2) \cdot r]}{[1 + (n-1) \cdot r]^2}. \qquad (27)$$

Frequency of dominant homozygotes *DD*:

$$d_n^2 = \frac{[1 + (n-2) \cdot r]^2}{[1 + (n-1) \cdot r]^2}. \qquad (28)$$

From these formulæ, the diagram, Fig. 9, and Table 2 have been drawn up. The diagram shows how the percentages for the different kinds of individuals are displaced in a population if the recessive character-bearers are always prevented from propagation. In the generation taken as starting-point, the recessive bearers have the frequency 25 %. To start with, they are eradicated very rapidly. No later than the fourth generation their frequency has dropped to 4 %. If, on the other hand, we begin with a population with 0.1 % character-bearers (30th generation in the diagram), in ten generations their frequency will have sunk not quite half (0.06 %). It is also noticeable that the effect on the heterozygotes is considerably weaker. Between the fourth and the ninth generation the recessive homozygotes are decreased from 4 % to 1 %, while on the other hand the heterozygotes decrease only from 32 % to 18 %. After 100 generations we have only 0.01 % character-bearers, but 200 times as many heterozygotes, that is to say 1.96 %. This means, then, firstly, that selection has a strong effect on the character-bearers at the beginning, but that these are never completely eradicated, and secondly, that the effect on the heterozygotes is appreciably less. Even after a very large number of generations and a selection of the strictest kind imaginable they may still be there in a low frequency. This agrees with our previous conclusion that, though the recessive character-bearers may be very rare, yet the heterozygotes are relatively numerous.

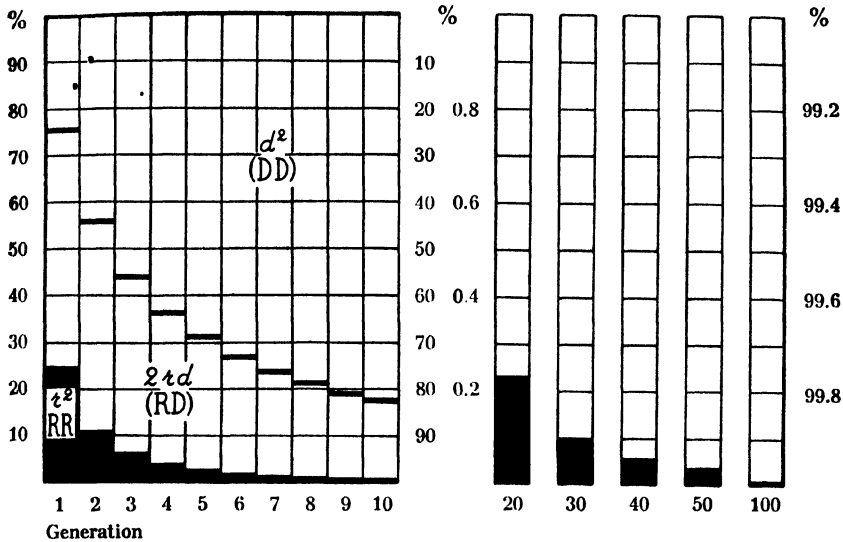


Fig. 9. Decreasing frequency of recessive character-bearers in successive generations when they are prevented from propagation.

TABLE 2.

Frequency of individuals of different genotypes in successive generations in monohybrid diallelism and total selection of recessive character-bearers. Cf. formulæ 26, 27 and 28.

Generation	RR	RD	DD
1	0.2500	0.5000	0.2500
2	0.1111	0.4444	0.4444
3	0.0625	0.3750	0.5625
4	0.0400	0.3200	0.6400
5	0.0278	0.2778	0.6944
6	0.0204	0.2449	0.7347
7	0.0156	0.2188	0.7656
8	0.0123	0.1975	0.7901
9	0.0100	0.1800	0.8100
10	0.0083	0.1653	0.8264
20	0.0023	0.0907	0.9070
30	0.0010	0.0624	0.9365
40	0.0006	0.0476	0.9518
50	0.0004	0.0384	0.9612
100	0.0001	0.0196	0.9803

In questions of selection, where the character-bearers are completely prevented from propagation, the thought of sterilizing measures is readily resorted to. The situation here is that a small group of members of the community are considered unsuitable as parents to a coming generation; consequently they are prevented from propagation. Before calculating the effect to be expected here, it should, of course, be known what the propagation of the group would presumably have been if left unsterilized. Further, it is necessary to know the type of heredity for the characters in question. Finally, the frequency of the different kinds of character-bearers composing the group must naturally also be known. The group is assuredly not uniform. (For example, there are certainly more than 10 types of hereditary blindness.) If, then, the group consists of a very large number of different character-bearers, each one of which is very rare, it is clear that the calculation cannot be made on the assumption of homogeneity in the group. The effect of selection on an extremely rare character comes very near to 0. If the measures are taken against several different kinds of rare character-bearers, the total effect will similarly be very small, and by no means as great as would doubtless have been if the group had been homogeneous and consisted of a single kind of character-bearer.

Analogous to the formulæ and the line of reasoning for recessivity it is fairly easy to work out formulæ for sex-linked inheritance. Therefore such formulæ are not given in this book. As an example it may be mentioned that the formula for total selection in sex-linked recessivity is:

$$r_n = \frac{r}{2^{n-1}(r+1)}, \tag{29}$$

where r_n is the frequency of the gene after selection in n generations, the first generation being that in which the effect of the selection is first apparent and which is a third after selection sets in.

We have now to investigate the effect of selection in more complicated inheritance. If a character is determined by two dominant genes, and if the one gene is assumed to have the frequency d' and the other the frequency d'', and if, further, $d' = id''$, in total selection after n generations the first gene will have the frequency

$$d'_n = \frac{d'}{1 + (n-1)\frac{d'}{i}}, \tag{30a}$$

and the second the frequency

$$d''_n = \frac{d''}{1+(n-1)\,id''}. \qquad (30b)$$

If $i = 1$, i. e. $d' = d'' = d$, the expression for both genes will be:

$$d_n = \frac{d}{1+(n-1)\,d}, \qquad (31)$$

which means that the process takes the same course as in monohybrid recessivity. The formula shows that if the one gene is more and the other less common, the frequency of the former will decrease slowly and that of the latter relatively quickly. In the extreme case where the one gene occurs in the entire population and the other has a lower frequency, this latter will disappear after one generation, after which the more common gene will maintain its subsequent frequency unchanged. In other complicated forms of heredity, the displacements will take place more slowly than in recessivity. In dihybrid recessivity, for example, the process must, if both genes are equally common, be appreciably slower than in monohybrid recessivity. If the one gene is common and is found in the whole of the population, and the other gene is not so common, the displacements will proceed as in monohybrid recessivity.

Partial selection.

In regard to selection it is customary to think exclusively of negative selection, e. g. measures aiming at decreasing or preventing the propagation of persons with a certain character. Obviously, however, negative selection also has a positive aspect. If one prevents the propagation of the possessors of a certain character, it implies that, relatively speaking, one favours the propagation of the ones who do not have the character. In England one generally speaks of positive and negative eugenic measures or factors, in Germany sometimes of selection and contra-selection. Anyhow, it is possible to calculate the effect of positive as well as of negative selection with the help of the same formulæ.

In establishing the formulæ for total negative selection, we have argued as though the gametes were mixed in the sea and united in a

random way to form zygotes. *Haldane* has given formulæ for partial negative selection, valid for aquatic organisms "which shed their gametes into water". If in each generation a proportion ($=k$) of the character-bearers are prevented from propagating and if this means that the frequency of a recessive gene, which was originally r, is decreased to r_n by the n^{th} generation, the frequency of the gene will be lowered by kr_n^2 in this generation, and there will also be a corresponding decrease for the total population. In the next generation, therefore, the character-bearers RR_{n+1} will have the frequency:

$$r_{n+1}^2 = \left[\frac{r_n - kr_n^2}{1 - kr_n^2}\right]^2. \tag{32}$$

The formula is, in fact, quite correct in lethal selection. With positive fertility selection the deviation is of great significance, but with partial negative selection the deviation is slight and with total negative selection the formulæ give the same result. We have spoken of "lethal" selection and "fertility" selection. The difference is of course that in the latter case the partner who is married to a character-bearer is also affected by the selection. In the former case the character-bearer dies.

To obtain a formula for fertility selection we assume that the frequency of heterozygotes cannot necessarily be deduced from the frequency of homozygotes as in panmixia. We assume that homozygotes for the recessive character when selection has been going on for n generations have the frequency $RR = a_n$ and that the dominant homozygotes then have the frequency $DD = c_n$; we further assume that the frequency of heterozygotes is $RD = b_n$.

The frequency of the different genotypes in the next generation is given in Table 3, when k of the recessive homozygotes are prevented from propagation[1]). By means of this table we obtain the following frequency of genotype in the next generation.

By means of this table the following recursion formula can be derived for the frequency of recessive homozygotes, a_{n+1}:

$$a_{n+1} = \frac{(a_n + b_n)^2 + k \cdot a_n \ (a_n + 2b_n)}{1 + k \cdot a_n \ (1 + 2b_n + c_n)}. \tag{33a}$$

[1]) If the propagation of the recessive character is $1 + k$, the propagation of the corresponding dominant character is $\frac{1}{1+k}$, the propagation of the recessive homozygotes being put as unity.

TABLE 3.

Cf. the text.

Combination of parents	Frequency in population	Children: Frequency of RR_{n+1}	Children: Frequency of RD_{n+1}	Children: Frequency of DD_{n+1}
$RR_n \times RR_n$	a^2	$a^2 + k \cdot a^2$		
$RR_n \times RD_n$	$4\,ab$	$2\,ab + k \cdot 2\,ab$	$2\,ab + k \cdot 2\,ab$	
$RR_n \times DD_n$	$2\,ac$		$2\,ac + k \cdot 2\,ac$	
$RD_n \times RD_n$	$4\,b^2$	b^2	$2\,b^2$	b^2
$RD_n \times DD_n$	$4\,bc$		$2\,bc$	$2\,bc$
$DD_n \times DD_n$	c^2			c^2
Total		$RR_{n+1} = (a+b)^2 + k \cdot a\,(a+2\,b)$	$RD_{n+1} = 2\,(b+c)\,(a+b+k \cdot a)$	$DD_{n+1} = (b+c)^2$
		$1 + k \cdot a\,(1 + 2\,b + c)$		

For heterozygotes b_{n+1} the formula is as follows:

$$2b_{n+1} = \frac{2\,(b_n + c_n)\,(a_n + b_n + k \cdot a_n)}{1 + k \cdot a_n\,(1 + 2b_n + c_n)} \tag{33 b}$$

and for dominant homozygotes c_{n+1} as follows:

$$c_{n+1} = \frac{(b_n + c_n)^2}{1 + k \cdot a_n\,(1 + 2b_n + c_n)}. \tag{33 c}$$

These formulæ have a general validity and can be used to compute the results of both positive and negative selection. If $k = 0$, there is no selection. If k is negative but < 1, partial negative selection is occurring; if $k = -1$, complete negative selection is occurring. If k is positive, positive selection is occurring. The formula is valid for selection affecting all recessive homozygotes. Their reproduction is helped or hindered irrespective of whom they are married to. If selection is negative for these cases it follows that it is positive for dominant homozygotes, when they marry one another. To deduce the effect of selection

acting on all the dominant homozygotes one may calculate the effect of selection acting only on unions between recessive homozygotes. The following expression is then obtained for the recessive homozygotes in the same way as above:

$$a_{n+1} = \frac{(a_n + b_n)^2 + k \cdot a_n^2}{1 + k \cdot a_n^2}. \tag{34a}$$

For heterozygotes the following expression is obtained:

$$2b_{n+1} = \frac{2\,(a_n + b_n)\;(b_n + c_n)}{1 + k \cdot a_n^2} \tag{34b}$$

and finally for dominant homozygotes the following expression:

$$c_{n+1} = \frac{(b_n + c_n)^2}{1 + k \cdot a_n^2}. \tag{34c}$$

These formulæ can be used to calculate the effect of partial negative selection and of positive selection on a dominant character. In the case of total negative selection, of course, the character disappears at once from the population.

It follows from these formulæ that negative selection always has a comparatively large effect on a recessive character which is rather common, but a smaller one on such characters when they are rare. We append tables to illustrate this. In the case of partial negative selection where the reproduction rate is half that of the rest of the population (i. e. $k = \frac{1}{2}$), the frequency will have fallen to 0.075% after 10 generations (cf. Table 4a). The effect of selection is, in other words, insignificant. If equally strong negative selection works against a dominant character with a frequency of 0.1% the effect will be that the frequency of the character will be reduced to 0.0001% (cf. Table 4a). Here, in other words, the effect is greater.

On the other hand, where positive selection operates the effect is powerful. If a recessive character has a frequency of 0.1% and the reproduction of all the individuals manifesting it is so favoured that it is double that of the rest of the population, the frequency of the character will have risen to nearly 0.2% after 10 generations (cf. Table 4b). In the case of all the dominant characters being favoured to the same extent, we get, after an equal number of generations, a rise to 34%

(cf. Table 4b). Of course, this strong effect of positive selection on very infrequent characters corresponds to a strong effect of negative selection on very frequent characters.

TABLE 4a.

The effect of partial negative selection during successive generations on recessive and dominant characters of different frequency by varying intensity, k, of the selection. Cf. formulæ 33 and 34.

Gen.	Frequency of recessive character			Frequency of dominant character		
	RR_0 = 0.1 % $k = -\frac{1}{2}$	RR_0 = 1 % $k = -\frac{1}{10}$	RR_0 = 1 % $k = -\frac{1}{2}$	$RD_0 + DD_0$ = 0.1 % $k = +\frac{1}{2}$	$RD_0 + DD_0$ = 0.1 % $k = +1$	$RD_0 + DD_0$ = 1 % $k = +1$
0	0.100	1.00	1.00	0.100	0.1000	1.00
1	0.097	0.98	0.91	0.067	0.0500	0.91
2	0.094	0.97	0.84	0.045	0.0250	0.83
3	0.091	0.95	0.77	0.030	0.0125	0.76
4	0.088	0.93	0.71	0.020	0.0063	0.69
5	0.086	0.92	0.65	0.013	0.0032	0.63
6	0.084	0.90	0.61	0.009	0.0016	0.57
7	0.081	0.89	0.56	0.006	0.0008	0.52
8	0.079	0.87	0.53	0.004	0.0004	0.47
9	0.077	0.86	0.49	0.003	0.0002	0.43
10	0.075	0.84	0.46	0.002	0.0001	0.39

TABLE 4b.

The effect of partial positive selection during successive generations on recessive and dominant characters of different frequency by varying intensity, k, of the selection. Cf. formulæ 33 and 34.

Gen.	Frequency of recessive character				Frequency of dominant character	
	RR_0 = 0.1 % $k = +1$	RR_0 = 1 % $k = +\frac{1}{10}$	RR_0 = 1 % $k = +\frac{1}{2}$	RR_0 = 1 % $k = +1$	$RD_0 + DD_0$ = 0.1 % $k = -\frac{1}{10}$	$RD_0 + DD_0$ = 1 % $k = -\frac{1}{2}$
0	0.100	1.00	1.00	1.00	0.100	0.10
1	0.106	1.02	1.08	1.17	0.111	0.20
2	0.113	1.04	1.19	1.39	0.123	0.40
3	0.120	1.05	1.30	1.68	0.137	0.79
4	0.128	1.07	1.43	2.05	0.152	1.55
5	0.137	1.09	1.58	2.53	0.169	3.00
6	0.147	1.11	1.75	3.18	0.188	5.65
7	0.158	1.13	1.94	4.06	0.209	10.11
8	0.170	1.16	2.17	5.26	0.232	16.77
9	0.183	1.18	2.44	6.91	0.257	25.20
10	0.199	1.20	2.75	9.17	0.286	34.16

Selection and mutations.

If, now, mutations appear in a population, and if the character-bearers arising thence are subjected to selection, the process must approach a state of balance, when the number of mutations correspond to the number of character-bearers disappearing as a result of selection. For example, in monohybrid recessivity if the gene has the frequency r and the mutations the frequency μ, a state of balance should be set up when $r^2 = 2\,\mu$.

The frequency of the heterozygotes, $2rd$, will then be:

$$2rd = 2\sqrt{2\,\mu}\,(1 - \sqrt{2\,\mu}).$$

If only k of the recessive character-bearers are prevented from propagation, we get the following expression:

$$r^2 = \frac{2\,\mu}{k}, \tag{35}$$

$$2rd = 2\sqrt{\frac{2\,\mu}{k}} \cdot \left(1 - \sqrt{\frac{2\,\mu}{k}}\right). \tag{36}$$

The expression within brackets is, of course, so near to 1 that it can be disregarded.

If the balance of the character-bearers is upset, there will be an increasingly slower return to it in subsequent generations, finally reached only after infinite time. The problem will be dealt with later, when we discuss processes which may upset a state of balance once attained.

We have hitherto assumed that selection and mutations occur in a population where panmixia otherwise obtains. If there are other deviations from panmixia, this may affect the processes, and we shall in the following pages therefore touch on selection and mutations again, in different connexions.

The first to try and compute the effect of selection was, as far as I can discover, *Warren* (1917), who carried out simple numerical calculations. The fundamental work in this field was carried out by *J. B. S. Haldane* (1924–1932). *Haldane* dealt with the problem from an evolutionary point of view, and used an intricate mathematical apparatus. The work was published in a littleread (at least outside England) periodical, and partly on this account no attention was at first paid to it in any wider circles. While *Haldane*'s work was still unknown to him, the present author had earlier submitted several basic formulæ and discussed their application to man (*Dahlberg*, 1926, and *Dahlberg-Hultkrantz*, 1927). Other authors, also not acquainted with *Haldane*'s work, since have sought to analyse the problem mathematically, for example *Bodewig* (1932–1933). Correct formulæ for positive and negative selection in human populations were given by *Dahlberg* (1946).

The effect of inmarriage on a population.

Reflection makes it plain that inmarriage i. e. marriage between relations encourages homozygosis and discourages heterozygosis. If, in a certain person, a mutation gives rise to a gene in recessive form, it can unite in homozygous form *only* through a marriage between the offspring, i. e. an inmarriage. The homozygotes there will be in later generations will all depend on consanguineous marriages, though the relationship between the individuals may not be close enough to be demonstrable.

Now, a population is composed of families and relatives. Consequently, when panmixia is assumed in a population, a certain amount of inmarriage must also be assumed to take place. If the population is large in relation to the separate families and their branches, then a stipulated panmixia means a comparatively small number of consanguineous marriages; if the reverse is the case, then it means a greater number. We should remember that the assumption of evolution implies that all individuals are related if the human race is taken to have evolved from a single mutation or from a small number whose offspring have been crossed. The same conclusion is reached if we calculate the ancestors of a given person for a large number of generations back. This would soon bring us to numbers far exceeding the conceivable size of the population of the earth at the time in question. Thus, if the ancestors are assumed not to have inmarried during the space of 30 generations back, their number will be 1000 millions, and 100 generations back, 10^{30} millions. This shows that losses of ancestors—that is to say consanguineous marriages—must have taken place to a very great extent during earlier generations. Even if the marriages are contracted at random, we must expect a greater or smaller number of inmarriages. The question then is: How great a deviation from normal panmixia do the consanguineous marriages occasion if they occur to a greater or less extent than is to be expected in panmixia? To solve this problem we must first get some gauge of the effect consanguineous marriages have.

The composition of the offspring in consanguineous marriages.

We will first calculate the composition of the offspring in the marriage of a brother and sister, in monohybrid diallelism. We assume that the recessive gene R has the frequency r; the dominant gene D therefore has the frequency $1-r$. A certain one of the four genes in the persons we start with has a chance of $\frac{1}{2}$ of getting as far as into a new generation, and again the chance of $\frac{1}{2}$ of getting into the next following generation. (Cf. Fig. 10.) Altogether, then the chance is $\frac{1}{4}$. That is

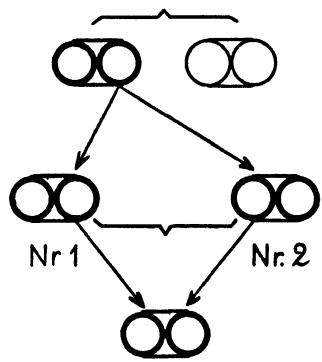


Fig. 10. Marriage of a brother and sister. The circles connected with two lines represent a gene pair.

to say, the prospect of this gene's encountering itself is $\frac{1}{4} \cdot \frac{1}{4} = \frac{1}{16}$. But we have four genes, which may all be the starting-point for a homozygote of this kind. The prospect will therefore be quadrupled, i. e. $4 \cdot \frac{1}{16} = \frac{1}{4}$. Thus in a fourth of the children, one of the primary genes will combine to form a homozygote, and in r cases the starting-point will be an R gene. This gives us a recessive character-bearer, because the primary gene encounters itself in $\frac{r}{4}$ of the cases. In the other $\frac{3}{4}$, the genes unite at random with one another, giving rise to a recessive homozygote. This should take place with the same frequency as an encounter of this kind has in the population, i. e. in r^2 of these $\frac{3}{4}$ of the cases. Altogether, we get character-bearers among the offspring from the marriage of a brother and sister in

$$\frac{1}{4}r + \frac{3}{4}r^2 \text{ cases.} \tag{37}$$

The probable frequency of character-bearers among the offspring from the marriage of cousins is calculated similarly. (Cf. Fig. 11.)

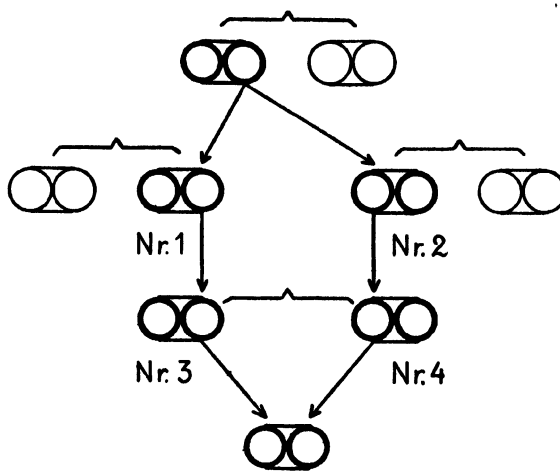


Fig. 11. Marriage of cousins. The circles connected with two lines represent a gene pair.

The chance that a certain gene goes to one of the children is $\frac{1}{2}$, for a grandchild it is $\frac{1}{4}$, and for a great-grandchild $\frac{1}{8}$. In the marriage of cousins, then, the prospect of a union of a certain gene in the offsprings with itself is $\frac{1}{8} \cdot \frac{1}{8} = \frac{1}{64}$. But we have four primary genes for such a union in the common paternal grandparents; these genes have the probability r of being R genes. The probability of a gene uniting with itself to give rise to a recessive character-bearer is therefore $4r \cdot \frac{1}{8} \cdot \frac{1}{8} = \frac{1}{16}r$. In the remaining $\frac{15}{16}$ of the offspring, character-bearers arise from random unions of genes with, on an average, the same chance as in the population, i. e. in r^2 cases. In all, then, the frequency of recessive character-bearers among the offspring in a marriage between cousins will be:

$$\frac{r}{16} + \frac{15\,r^2}{16}, \tag{38}$$

and the frequency of dominant character-bearers:

$$d^2 + 2\,rd - \frac{1}{16}\,rd. \tag{39}$$

The composition of large populations under inmarriage.

Let us assume that we are dealing with a very large population. Relatively, therefore, the separate families and branches are extremely small, so that in panmixia we must only expect an extremely small number of marriages between cousins, approaching 0. If a character is determined by recessive monohybrid diallelism, and the R gene has the frequency r, we get recessive character-bearers with the frequency r^2.

We now assume that only marriages between cousins are contracted in the population. In this case it will have the composition $\frac{1}{16}r + \frac{1}{15}r^2$, according to the equation deduced above. This extremely intensive inmarriage will raise the frequency of the recessive homozygotes thus:

$$\frac{1}{16}r + \frac{15}{16}r^2 - r^2.$$

Simplified, this gives:

$$\frac{1}{16}(r - r^2) = \frac{2rd}{32}. \tag{40}$$

This expression shows that the heterozygotes are decreased by $\frac{1}{16}$, and that half of this decrease, $\frac{1}{32} = 3.13\,\%$ of the heterozygotes, is met by an equal increase of recessive and dominant homozygotes respectively. The increase reaches its maximum when $r = \frac{1}{2}$. We then have 25 % recessive character-bearers in panmixia. When there is nothing but marriage between cousins, a further $\frac{1}{64}$ (i. e. 1.56 %) of the population will be character-bearers, giving us instead 26.56 %. If the gene is rarer, the displacement of the population's composition which this extreme inmarriage occasions will be even less. (See Table 5 and Fig. 12.) The diagram shows how the effect of inmarriage slowly increases to a maximum at $r = \frac{1}{2}$, and then gradually diminishes. Fig. 13 illustrates the increase in a rising percentage of character-bearers in the population.

The diagrams and table show that there is a comparatively unimportant displacement of the composition of the population even in this extreme situation when there is only marriage between cousins. Now, inmarriage can never reach such high degrees in a human population. According to official statistics, we can rather reckon with an in-

TABLE 5.

Increase of the percentage of recessive, monohybrid character-bearers in increasing frequency of a recessive gene in a population where only marriages between cousins are contracted.

Frequency of the gene in a population	Frequency of the character-bearers in a population in panmixia	Increase of the number of character-bearers in a population where only marriages between cousins are contracted
0.001	0.0001	0.000619
0.1	0.01	0.00562
0.2	0.04	0.01000
0.3	0.09	0.01313
0.4	0.16	0.01500
0.5	0.25	0.01562
0.6	0.36	0.01500
0.7	0.49	0.01313
0.8	0.64	0.01000
0.9	0.81	0.00562

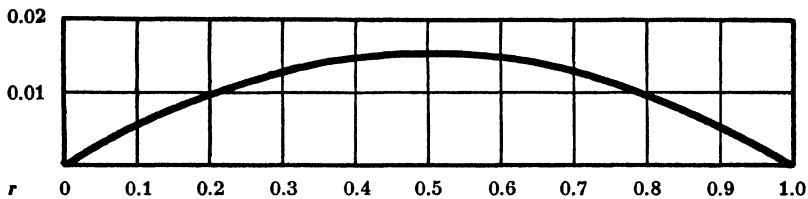


Fig. 12. Increase of the frequency of monohybrid, recessive character-bearers in a population where only marriages between cousins are contracted, compared with panmixia when the percentage of genes is increasing. To make the curve clearer the scale has been made ten times larger in vertical direction than horizontally.

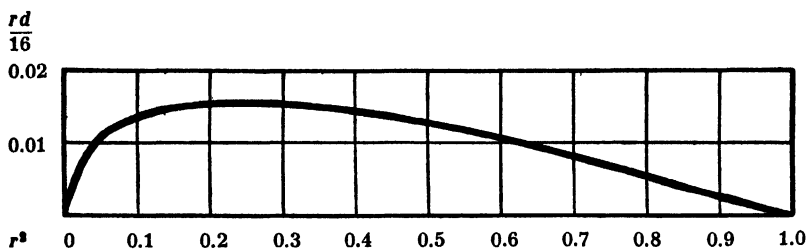


Fig. 13. Increase of the frequency of monohybrid, recessive character-bearers in a population where only marriages between cousins are contracted, in comparison with panmixia when the proportion of character-bearers is increasing. To make the curve clearer the scale is ten times larger in vertical direction than horizontally.

marriage frequency of at most about 1 % marriages between cousins, and 0.075 % marriages between parents' brothers and sisters and their children. And even if these latter marriages give rise to a somewhat greater increase (twice as intensive) as the marriages between cousins, it must nevertheless be taken into account that, with the frequencies and degrees that inmarriage can reasonably be thought to have in human populations, it should not appreciably change the constitution of the population, compared with panmixia. In other words, the changes we can expect are so mild that for a single character they can hardly be demonstrated statistically. No doubt the sources of error which are inevitably bound up with all population statistics are usually large enough to prevent us from demonstrating in any single instance such differences as are under discussion here.

The composition of a population in inmarriage in small populations.

It is conceivable that a population may be so small as to lead one to expect a comparatively large number of consanguineous marriages in panmixia, but that for some reason these are not forthcoming. We will again choose an extreme example. Let us assume a population where, in panmixia, we would expect marriages to be in a certain frequency, a, between brother and sister. If $a = \frac{1}{10}$ and if families have the same number of children of marriageable age, say two, the population will consist of about ten families. Now, there are no marriages between brother and sister in these populations, and this sets up a deviation from the populational composition to be expected from panmixia. If the recessive gene R has the frequency r, we get r^2 recessive character-bearers in panmixia. In marriages between brother and sister the composition of the offspring is, as we have already shown, $\frac{1}{4}r + \frac{3}{4}r^2$. In panmixia, a of the population have, in this case, this composition. We will assume that the remaining $1-a$ have the composition x. This gives us the following equation:

$$r^2 = a\left(\frac{1}{4}r + \frac{3}{4}r^2\right) + (1-a)\,x.$$

If this is solved, we get:

$$x = \frac{4r^2 - ar - 3ar^2}{4\ (1-a)}.$$

If marriages between brother and sister are not contracted, the population will have the same composition as that part where such marriages do not occur. If we want to make a comparison with complete panmixia, we obtain the decrease in the number of the recessive character-bearers, $\Delta\ x$, from the formula:

$$\Delta x = x - r^2,$$

$$\Delta x = \frac{a(r^2 - r)}{4\ (1-a)} = -\frac{ard}{4\ (1-a)}. \tag{41}$$

This expression is 0 when $r = 0$ or $r = 1$. Between these two, the expression is negative, which implies that the non-contracted marriages between brother and sister cause a decrease of the recessive character-bearers. This decrease is maximal if $r = \frac{1}{2}$; if, for example, $a = \frac{1}{10}$, the decrease is then 1.39%. In this case, then, we get 23.61 % recessive character-bearers, instead of 25 %. Thus, although the population concerned is extremely small, the maximal decrease that the non-contracted marriages between brother and sister set up is of small importance. It should further be remembered that for rarer genes the increase is even less noticeable. It can also be stated that, if the size of the population in relation to that of the family leads one to expect 1 % of marriages between brother and sister in panmixia, the nonfulfilment of these marriages will occasion a maximal decrease of 0.12 % in the number of character-bearers. If there are two children, the population will then comprise about 50 families, or approximately 100 individuals.

These calculations show that, even with comparatively small populations and fairly common characters, a nonfulfilment of marriages between brother and sister will make for a relatively slight difference in the proportion of a certain kind of character-bearer, compared with panmixia. The examples we chose to demonstrate this are probably far more extreme than what we can expect in human populations, apart from extremely rare exceptions. As, for such popu-

lations, inmarriage is a reasonably unimportant phenomenon, we can probably maintain that it has no noticeable importance for the normally experienced size of a population. As will be shown later, we have reason to assume that the size of a "population" in Western Europe amounts to several hundreds of individuals.

We have carried out our calculations solely for marriages between brother and sister, though such marriages are never contracted in human populations. The effect of any other non-contracted consanguineous marriages is considerably less than it is for the brother and sister marriages and we can certainly expect to find no very marked abstention from these marriages. There is hardly reason to suppose that cousins marry one another to any appreciably greater or lesser extent than other persons in the population, who are not related (cf. below). Marriages between cousins and other relations (apart from brothers and sisters and parents and children, which last should, however, be very rare in panmixia on account of the difference in age) can therefore, in many populations, be assumed to occur to about the same extent as is to be expected in panmixia, taking into account the size of the population. Deviations (which will be discussed later) will doubtless be of very low numerical value.

Inmarriage and complicated mechanisms of heredity.

The conclusions drawn apply to monohybrid diallelism, but they also hold good for other forms of recessive inheritance. It is possible to show that the effect of inmarriage in dihybrid diallelism on the frequency of certain character-bearers is less than in the case of monohybrid diallelism. The effect will be smallest when both the genes are equally common; it will be stronger when one gene is commoner than the other, and will reach its maximum if the one gene is present in practically all of the population, in which case we more or less have monohybrid diallelism. In higher forms of polyhybridity the effect becomes even slighter. We can say that the effect of inmarriage is more powerful the rarer the genes are, and at a certain frequency of character-bearers we get the highest degree of rarity if there is monohybridism.

It now remains to deal with the question of the effect of inmarriage in dominance. In monohybridism, dominance can be said to be the reverse of recessivity. The increase of recessive character-bearers is ob-

tained at the expense of the dominant character-bearers. It must, however, also be remembered that if a recessive gene is rare, the corresponding dominant gene is common, and vice versa. Now, if the recessive gene is common, we get no statistically noticeable change of the population constitution from inmarriage. This implies that the same is true in the case of rare dominant genes. If a recessive gene is rare, there is also no noticeable change of the population's composition, which similarly implies that this last is not affected by consanguineous marriage, even in questions of common dominant genes. We can draw the same conclusions for different forms of polyhybridism. Inmarriage is of no consequence for the character-bearers who are determined by recessive genes, whether these last are rare or common, and it is also of no consequence for polyhybrid dominant genes.

Hitherto we have discussed inmarriage with reference to the separate characters. But inmarriage affects simultaneously all rare genes, and the total effect cannot be summarily dismissed. We shall be returning to this question in a subsequent chapter where the frequency of inmarriage among the parents of character-bearers will be dealt with.

The usual idea probably is that inmarriage is very important, since its intensive practice in breeding animals gives a very powerful effect. Here brothers and sisters are consistently mated generation after generation. In such matings, the heterozygotes disappear relatively quickly, as was shown by *Sewall Wright* (1921) for one. Even if inmarriage has, in principle, the same effect in man, i. e. sets up a diminished heterozygotism, the effect displayed here is very much less, as in practice only marriages between cousins occur in a relatively small frequency, and such marriages repeated generation after generation are so rare that such matings lack importance.

Formulæ for human populations have been presented by the author (*Dahlberg*, 1929). Subsequently, *Hogben* (1933 a) has calculated formulæ for more removed degrees of inmarriage. These calculations are laborious, and *Hogben* has provided a simple way of arriving at the formulæ.

Inmarriage from the point of view of the character-bearers.

It has been stated above that inmarriage is of importance for the frequency of very rare recessive characters. From this it follows that, if we take rare character-bearers as starting-point, we find that their

parents are very frequently cousins. As early as 1919 *Lenz* deduced an equation for calculating the frequency to be expected in different frequencies of a monohybrid diallelous character. The deduction is only approximate, however; *Lenz* only takes heterozygotes and disregards homozygotes, and he also disregards the fact that a number of marriages between cousins are to be expected in panmixia. The correct equation for large populations has been given by *Dahlberg* (1929).

Let us assume that the gene has the frequency r and the marriages between cousins the frequency c. The frequency of marriages not between cousins will then be $1-c$. If we assume the population to be very large, so that in panmixia there would be practically speaking no marriages between cousins, c then implies an increase of such marriages beyond what is to be expected in panmixia.

From marriages between cousins are derived character-bearers with the following frequency:

$$\frac{cr}{16}(1+15r).$$

In the population there are character-bearers with the following frequency:

$$(1-c)\,r^2+\frac{cr}{16}(1+15r).$$

The ratio of character-bearers derived from marriages between cousins to that of the total number of character-bearers, k, will be:

$$k=\frac{\frac{cr}{16}(1+15r)}{(1-c)\,r^2+\frac{cr}{16}(1+15r)};$$

$$\therefore k=\frac{c}{c+\frac{16\,(1-c)\,r}{1+15r}}. \qquad (42)$$

If c is a very small number in this equation, we can put $1-c=1$, and if we also venture to put $1+15r=1$ (which is very doubtful), the equation will be as follows:

$$k=\frac{c}{c+16r}. \tag{43}$$

This is the approximate equation that *Lenz* deduced (cf. also *Hogben*, 1933 b).

If we assume that marriages between cousins actually do occur with a certain frequency, c_1, and are to be expected in panmixia in a certain frequency, c_2, character-bearers from marriages between cousins will have the following frequency:

$$\frac{c_1 r}{16}(1+15r).$$

In the population we should, in panmixia, expect character-bearers with the frequency r^2. But we get an increase of their frequency by

$$(c_1-c_2)\frac{r}{16}(1+15r).$$

In all, then, the frequency of character-bearers in the population will be:

$$(1-c_1+c_2)r^2+(c_1-c_2)\frac{r}{16}(1+15r).$$

Therefore, the ratio of character-bearers from cousins to the total number will be:

$$k=\frac{\frac{c_1 r}{16}(1+15r)}{(1-c_1+c_2)r^2+(c_1-c_2)\frac{r}{16}(1+15r)};$$

$$\therefore k=\frac{c_1}{c_1-c_2+\frac{16r(1-c_1+c_2)}{1+15r}}. \tag{44}$$

If $c_2 = 0$, i.e. if the population is so large that the random frequency of cousin marriages to be expected is small enough to be ignored, we get formula 43, if we also set $1 + 15r = 1$, which implies a very doubtful approximation. If $c_1 = c_2 = c$, i.e. if the marriages between cousins occur in the frequency to be expected in panmixia, the equation will be:

$$k = \frac{c\,(1 + 15\,r)}{16\,r}. \tag{45}$$

TABLE 6.

Proportion of character-bearers (in per cent) deriving from marriages between cousins $= k$, in different frequencies of a recessive, monohybrid, diallelous character RR and in different frequencies of marriages between cousins in a population $= c$. Cf. formula 45.

RR	k when			
	$c = 0.1\,\%$	$c = 0.25\,\%$	$c = 0.5\,\%$	$c = 1\,\%$
0.000001	6.344	15.860	31.721	63.439
0.00005	0.978	2.444	4.888	9.776
0.0001	0.719	1.797	3.594	7.188
0.0005	0.373	0.933	1.866	3.733
0.001	0.291	0.729	1.457	2.912
0.0025	0.219	0.547	1.094	2.188
0.005	0.182	0.455	0.911	1.821
0.01	0.156	0.391	0.781	1.563
0.05	0.122	0.304	0.609	1.217
0.1	0.114	0.284	0.568	1.135

Table 6 and Fig. 14 give figures for the percent of character-bearers deriving from marriages between cousins in different frequencies of a recessive monohybrid diallelous character and of such marriages. The approximate formula 43 gives slightly lower values than the correct formula 45, if we assume that marriages between cousins occur to the same extent which one should expect in panmixia. For very rare genes and particularly in small populations with a high frequency of cousin marriages, the difference is not negligible. For instance, where the ratio for the gene is 1 : 10 000, and the proportion of cousin marriages is 1 per cent, we find by the approximate equation that the number of cousins among parents of character-bearers is 5.88 per cent, whereas the true figure is 7.19 per cent. The differences can thus sometimes be substantial ones.

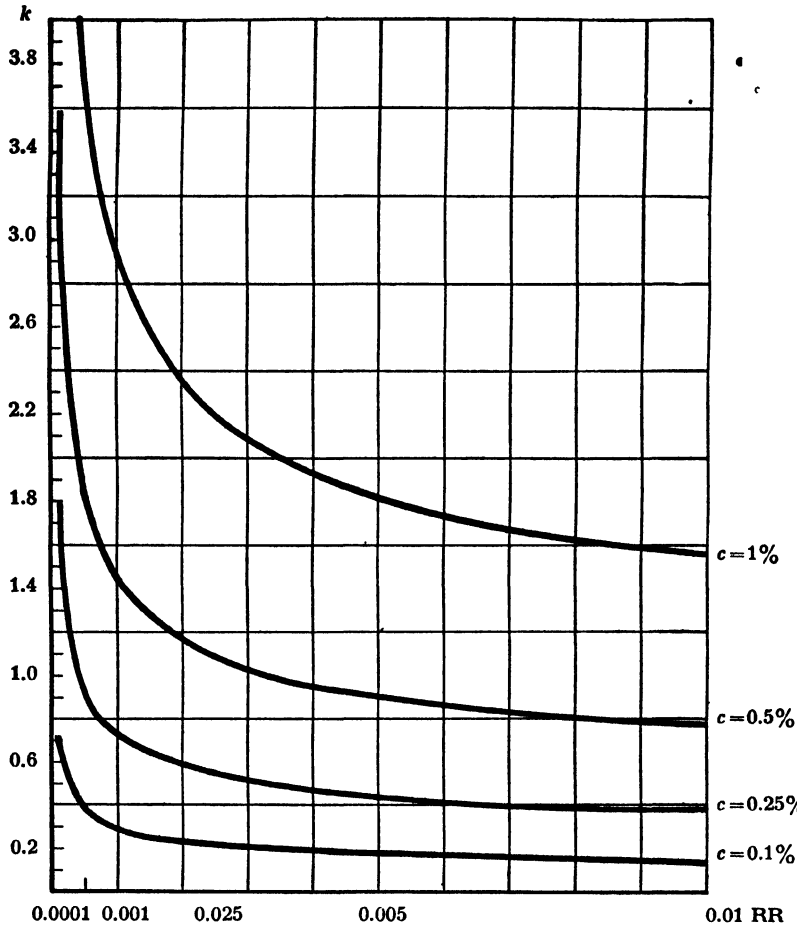


Fig. 14. Proportion of character-bearers (in per cent) deriving from marriages between cousins (k) in populations where the frequency of marriages between cousins (c) and the frequency of a recessive character is varying. Cf. Table 6.

It may also be mentioned in this connexion that a similar increase is to be expected in more complicated forms of inheritance. (In dihybrid dominance, when the two genes are equally common, the increase is maximally equal to that in monohybrid recessivity; when the one gene is common and the other rare, we have an extremely slight increase of marriages between cousins in the parents.) Indeed, when we want to prove that hereditary factors play a part in the

appearance of such characters as diseases and the like as are relatively rare, we can pursue two lines. We can demonstrate an increased frequency of the character in near relations of the character-bearer (brothers and sisters, parents, children, etc.) and we can also show an increased frequency of consanguineous marriages between the parents of the character-bearers. This latter line has been followed to a certain extent, but should be used still more, since an increased frequency among the relations may be connected with environmental factors. That tubercular parents have children suffering from tuberculosis may, for example, be due to infection. On the other hand, an increase in the inmarriage frequency in parents of tubercular children may not be connected with anything other than hereditary factors, and is therefore of greater value as proof.

It is of interest to try and get some idea of the rise to be expected in polyhybrid inheritance. Let us assume that a recessive polyhybrid character is composed of the genes $R_1\ R_1$, $R_2\ R_2$, ... $R_n\ R_n$ with the frequencies r_1^2, r_2^2, ... r_n^2. Let us assume further that for each pair of genes, marriages between cousins cause increases of δ_1, δ_2, ... δ_n. In panmixia we would expect character-bearers to have the frequency r_1^2, r_2^2, ... r_n^2. On account of inmarriage we get $(r_1^2 + \delta_1)$, $(r_2^2 + \delta_2)$, ... $(r_n^2 + \delta_n)$. If we now go on to assume that inmarriage in panmixia is to be expected with a frequency of c_1 and occurs in the population with the frequency of c_2, that proportion of the character-bearers, k, deriving from cousins, will be:

$$k = \frac{c\,(r_1^2 + \delta_1)\,(r_2^2 + \delta_2) \ldots (r_n^2 + \delta_n)}{(1 - c_1 + c_2)\,r_1^2\,r_2^2 \ldots r_n^2 + (c_1 - c_2)\,(r_1 + \delta_1)\,(r_2 + \delta_2) \ldots (r_n + \delta_n)}.$$

If there is dihybridism, for example, and if $r = r_1 = r_2 = r_3$ etc., the formula will appear as follows:

$$k = \frac{c}{c_1 - c_2 + \dfrac{(1-c)^2\ 256\ r^2}{(1 + 15\,r)^2}}. \qquad (46)$$

We may remind readers that character-bearers in this case have the frequency r^4. The formulæ show that when more marriages occur between cousins than is normal in panmixia with a given frequency of character-bearers the increase to be expected is lower in dihybrid

or polyhybrid recessivity than in monohybrid recessivity. It is further seen that that proportion of character-bearers deriving from marriages of cousins is also less in polyhybridism than in monohybridism. We may remember in this connection that *Haldane* (1938) showed that if there is monohybrid triallelism and a gene in homozygous form is the lethal factor, then we get a lower proportion of character-bearers from marriages between cousins and lesser increase from such marriages than we would expect here. A mechanism of this sort has not as yet been established in human populations, however.

It may finally be asserted that if the inheritance mechanism and the frequency of cousin marriages between the parents of character-bearers is known, the equations submitted here can, of course be used to calculate the frequency of the genes. If, for example, 15 % of the character-bearers are cousins, and the general frequency of marriages between cousins is 2 %, the gene will have the frequency 1 : 105, and if the general frequency of cousin marriages is 1 %, the gene will have the frequency 1 : 225, or 0.44 %. If the general frequency of cousin marriages is 0.5 %, the corresponding figures will be 1 : 465, or 0.22 %. With knowledge of the mode of inheritance, the frequency of the character-bearers, and the proportion of these latter deriving from cousins, it is of course also possible to calculate the frequency of the marriages between cousins in the population.

One reason why the frequency of inmarriage has not been very extensively investigated nor used in genetic research is the difficulty of getting normal figures. There are official figures from a number of countries (cf. *Dahlberg*, 1938). But they cannot by themselves be used for comparison with materials collected in other populations, even though they may be thought to provide an approximate starting-point. We can probably assume that the frequency of inmarriage seldom exceeds 1 %, and, at present, probably not infrequently keeps well below $\frac{1}{2}$ %. We shall be returning to this question later.

It may be pointed out in this connexion that figures obtained from patients treated at hospitals are not representative for the conditions in a population. The patients naturally include a number of cases of hereditary diseases, the parents of these cases having a considerably higher inmarriage frequency. Even if the group is small, it nevertheless tends to raise the average figure. *Julia Bell* (1940) has submitted figures from patients treated in English hospitals and reached

a figure of 0.61 % marriages between cousins. This seems an unexpectedly high figure for a country like England, where the communications are good and where the isolates are probably relatively large. If we assume that the real figure for the population is 0.25 % and that the material includes a number of persons suffering from rare hereditary diseases, whose parents are cousins in 10 %, for example, we can calculate that this group should constitute 3.7 % of the material. It is in itself not unreasonable to assume that the sum of rare hereditary diseases amounts to one or two more percent, i. e. that children from marriages between cousins are over-represented (longer time of treatment), and that this means that the material is of doubtful value as a basis for a discussion of the conditions in the population.

Linkage and inmarriage.

In panmixia we should expect characters to occur together at random in the same person. If there is linkage, they should occur together more often. In other words, there should be a correlation between the occurence of certain hereditarily determined characters. Recent genetical research has been greatly concerned with linkage in man, and special methods have been worked out to establish linkage in investigations of families and among siblings.

In the present work, the study of the problem is limited to the constitution of entire populations. As regards linkage, we can then content ourselves with stating that correlations between the occurrence of characters may be due to linkage. They may also be due to something else, however. We shall be returning to this problem later. In this connexion we shall only discuss the correlation that may be due to inmarriage.

When we want to investigate how characters occur together in a population, we must also take into account that the population falls into two groups: offspring to closely related persons, and others. In this connexion we will only take marriages between cousins into account, and disregard other consanguineous marriages, since, as has been maintained before, it is rare to find a closer kind with a powerful effect, and marriages between more distant relatives cause a very much smaller increase of homozygosis. Now, recessive characters have a different frequency in these parts of the population. Among

offspring from marriages between cousins the frequency is higher for rare characters than among offspring from other marriages. The probability that two rare non-linked characters will occur together is therefore larger among the offspring of cousins than among those of persons who are not cousins. If we now calculate how often character-bearers ought to coincide on the basis of their frequency in the whole population, and investigate how often they actually do coincide, we find an increase implying a correlation between the characters.

Let us assume marriages between cousins in the population with a frequency c, so that other marriages have the frequency $1-c$. Let us further assume that two recessive characters have the frequency p_1 and p_2, and, finally, that k_1 of the character-bearers derive from cousins for the character p_1, and k_2 for the character p_2. The frequency of character-bearers among offspring from marriages between cousins is

$$\frac{p_1 k_1}{c} \text{ and } \frac{p_2 k_2}{c}$$

respectively, and among the rest of the population

$$\frac{p_1 (1-k_1)}{1-c} \text{ and } \frac{p_2 (1-k_2)}{1-c}.$$

We would expect the character-bearers to meet at random in the frequency $p_1 p_2$. Actually they meet in the frequency:

$$\frac{p_1 p_2 (1-k_1)\ (1-k_2)}{1-c} + \frac{p_1 p_2 k_1 k_2}{c}.$$

The ratio between actual and expected frequency is thus:

$$y = \frac{(1-k_1)\ (1-k_2)}{1-c} + \frac{k_1 k_2}{c}. \tag{47}$$

Table 7 and Fig. 15 show the importance of inmarriage for the coincidence of characters. The figures have been calculated on the assumption that $p_1=p_2$, and also $k_1=k_2$. The effect is stronger the

TABLE 7.

Meeting of two recessive, monohybrid, diallelous characters (y) with the same frequency, when the frequency of marriages between cousins (c) and the proportion of character-bearers deriving from such marriages (k) varies. (This depends on the varying frequency in the population of the character-bearers.) Cf. formula 47.

k, %	y when			
	$c = 0.001$	$c = 0.0025$	$c = 0.005$	$c = 0.01$
1	1.081	1.023	1.005	1.000
2	1.361	1.123	1.045	1.010
3	1.842	1.303	1.126	1.040
4	2.523	1.564	1.246	1.091
5	3.403	1.905	1.407	1.162
10	10.811	4.812	2.814	1.818
15	23.223	9.724	5.226	2.980
30	90.491	36.491	18.493	9.455

lower the frequency of the marriages between cousins and the greater the proportion of the character-bearers deriving from such marriages. As has already been shown, this proportion is greater the rarer the character and the greater the frequency of the marriages between cousins. By using the figures in Tables 6 and 7 we get an orientation. If, for example, we assume that the marriages between cousins have the frequency of 0.25 %, which seems to be a reasonable figure, we find a noticeable effect in the form of an increased correlation, when over 2 % of the character-bearers come from such marriages; this means a character frequency of somewhat less than 1 in 10 000. If the cousin marriages have the frequency of 0.5 %, we get a marked effect in a frequency of character-bearers of somewhat more than 1 in 10 000. By using formulæ 46 and 47, we can, finally, calculate the relation between actual frequency and the frequency to be expected in panmixia for the meeting of the characters, if the respective genes have the frequency r_1 and r_2, and if the frequency of cousin marriages is c and corresponds to the one to be expected in panmixia. The formula will then be:

$$y = \frac{\left(1 - \frac{c\,(1 + 15\,r_1)}{16\,r_1}\right)\left(1 - \frac{c\,(1 + 15\,r_2)}{16\,r_2}\right)}{1 - c} + \frac{c\,(1 + 15\,r_1)\,(1 + 15\,r_2)}{256\,r_1\,r_2}. \qquad (48)$$

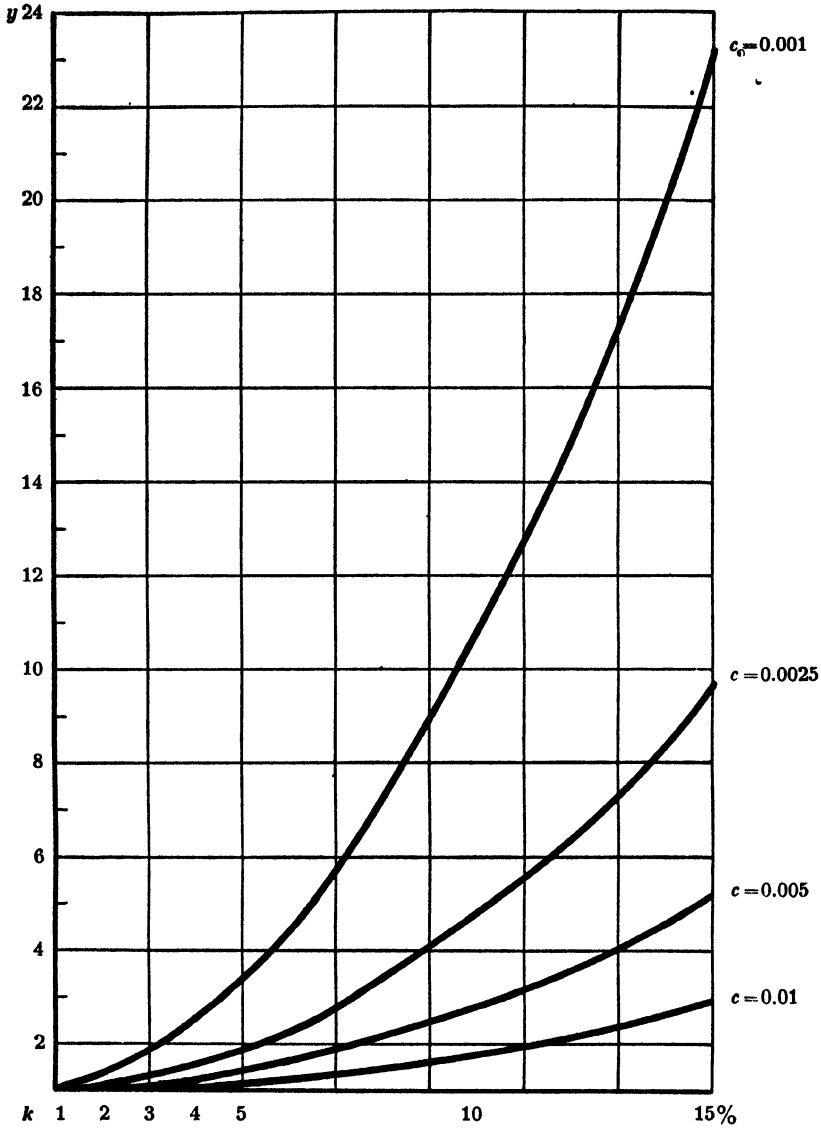


Fig. 15. Meeting of two recessive characters (y) with the same frequency in the population, in different frequencies of marriages between cousins and varying proportion of character-bearers deriving from such marriages (k). Cf. Table 7.

Using this formula some values have been worked out in Table 8, on the assumption that $r_1=r_2=r$. It is seen that the quotient more noticeably

TABLE 8.

Meeting of two recessive, monohybrid, diallelous characters (y) with the same frequency, in different frequencies of marriages between cousins (c) and varying frequency of character-bearers (RR). Cf. formula 48.

RR	y when							
	c = 0.001		c = 0.0025		c = 0.005		c = 0.01	
0.000001	k, 6.3	4.902	k, 15.9	10.771	k, 31.7	20.591	k, 63.4	40.378
0.00005	%1.0	1.077	% 2.4	1.193	% 4.9	1.387	% 9.8	1.778
0.0001	0.7	1.038	1.8	1.096	3.6	1.192	7.2	1.387
0.0005	0.4	1.008	0.9	1.019	1.9	1.038	3.7	1.075
0.001	0.3	1.004	0.7	1.009	1.5	1.018	2.9	1.037

exceeds 1 when the frequency of the character-bearers is 1 in 10 000, or lower. At a certain frequency of the gene the effect is more marked the higher the frequency of cousin marriages. It is plain that we must expect a correlation between characters primarily for rare genes, and with very rare characters we can obtain an extremely strong effect. So from these calculations we may conclude that only in very rare genes is it possible to determine a decidedly greater frequency in the coincidence of characters in one and the same person due to marriages between cousins. The effect is of no importance for common characters.

It must be remembered here that, with rare characters, the effect concerns all characters inherited recessively or in a more complicated way. Actually, an effect of this kind might explain why various sorts of malformations are relatively often found in the same person. A number of malformations are due to intra-uterine, environmental factors or to genes which cause injuries to several organs at the same time. However, the literature on hereditary malformations contains reports of the coincidence of independent characters, e. g. syndactylia, polydactylia, palatoschisis, congenital defect of the heart, etc. Such correlation may indicate linkage, but the difference in character of the hereditary malformations which are correlated may imply that marriages between cousins play a decisive part. The problems have not been studied in more detail from the viewpoints applied here, however, so that no definite statement can be made.

Naturally, inmarriage is also of importance as regards the frequency of the character in the siblings of the bearer. There is an

increased homozygosis for rare hereditary characters among children from marriages between cousins. When selecting character-bearers deriving to a special extent from such marriages, it is to be expected that their brothers and sisters will display increased frequency of other rare recessive characters. A correlation of this kind between brothers and sisters cannot therefore summarily be interpreted as indicating linkage. *Luxenburger* (1927) has, for example, tried to show a higher frequency of tuberculosis among the relations of certain mental cases (schizophrenes) than would be expected from a random estimate. His investigations have been keenly criticized (*Alström*, 1942). All the same, the problem is not fully worked out, even if the figures submitted by *Luxenburger* are unsound. If hereditary factors play a part both for tuberculosis and schizophrenia, marriages between cousins may set up a correlation between the characters within the brother-and-sister circles, provided the genes are sufficiently rare. This mechanism, hitherto disregarded, may also be of importance when it is desired to show linkage through family investigations; as has been stated above, however, this problem falls outside the province of this work.

Summing up, it may be said that inmarriage has no importance for ordinary characters. It plays a larger part for rare recessive or complicatedly hereditary characters, and in extreme cases, when a gene appears for the first time as a mutation, this gene can meet in homozygous form only through marriage between descendants of the individual with the mutated gene, i.e. through consanguineous marriage. If a character is rare, it is of no noteworthy importance for the composition of the population, however. The effect of inmarriage is counterbalanced by the frequency of the genes, so that inmarriage never makes for noteworthy importance of a single character in a population. Thus, while selection has a considerable effect on ordinary characters but has no appreciable importance for very rare ones, the situation is the reverse for inmarriage: in this case ordinary characters are not affected, but rare ones very much so *from the point of view of the character-bearers*. Selection only affects single rare characters, whereas a change of the frequency of inmarriage brings about, on the other hand, a change in the frequency of *all* rare characters. The total effect may be important from the viewpoint of society. These aspects will be followed up in connexion with the subsequent discussion on the effect of inmarriage and isolate boundaries.

As inmarriage effects the frequency of the rare characters, we would expect the parents of rare character-bearers to be related (cousins) to a comparatively large extent. Conversely, we expect a correlation between the occurrence of rare characters, because, when choosing such, we start from persons who to a relatively large extent are cousins, and among whose offspring we would expect an increase of rare character-bearers.

Inmarriage and selection.

It has been stated earlier on that a certain frequency of inmarriage is to be expected in panmixia. We have furthermore given formulæ for the effect of selection in panmixia. The question then is, what effect on the selection process has a frequency of inmarriage higher or lower than the one to be expected in panmixia? A human population contains both possibilities in so far as, in a number of populations, the frequency of marriages between cousins is lower than would be expected in panmixia, because such marriages are more or less forbidden. A somewhat higher frequency of such marriages than that corresponding to panmixia is probably to be found in populations where the marriage is arranged by the parents of the pair. In other words, both aspects of the problem are of practical interest.

In the first place, then, we ask what importance the absence of marriages between cousins can be thought to have. If they are perpetually prevented, and would, in panmixia, have the frequency c, the population will have the following composition:

$$r^2 - c\left(\frac{r}{16} + \frac{15\,r^2}{16}\right).$$

The part that drops out is thus:

$$c\left(\frac{1}{16}r + \frac{15}{16}r^2\right) \tag{49}$$

or, relative to r^2:

$$c\left(\frac{1}{16\,r} + \frac{15}{16}\right).$$

If the marriages between cousins increase beyond what is to be expected in panmixia, the same equations apply, but the sign before c must be reversed. The increase or decrease of character-bearers which is to be expected at different values of c and r^2 is easy to obtain from the formulæ.

It must be remembered that a decrease compared with panmixia cannot be greater than the frequency of marriages between cousins to be expected in panmixia, while, on the other hand, the increase theoretically can be 100 %.

The expressions in the table show that, in accordance with what has been shown before, marriage between cousins is not of importance for the frequency of character-bearers until the gene is rare in a population; we also see that the effect sets in earlier when there is a larger change in the frequency of marriages between cousins compared with panmixia, than if the change is small. In principle, this means that the effect of selection will be larger on rare characters when such marriages occur more often than in panmixia. The increase they give is, however, of no fundamental importance in so far as when the frequency of marriages between cousins is as high as 1 %, an increase of the bearers by 63 %, i. e. rather over half, is obtained only when the frequency of the character-bearers is about 1 : 1 000 000. At a certain mutation frequency, deviations in the frequency of inmarriage will have a certain importance for the state of balance reached. That is to say, the heterozygous frequency corresponding to the state of balance will be somewhat higher if inmarriage occurs to a lesser extent than would be expected in panmixia, and will be somewhat lower in the opposite case. However, the displacement is probably of no very great importance in human populations. We shall be returning to the problem in connexion with the discussion of the effect of isolates.

Assortative mating.

Assortative mating denotes crossings between persons with certain characters to a greater extent than one would expect at random; thus, crossings of the opposite sort to a corresponding extent have a lowered frequency. No very detailed investigations of the extent of assortative mating in man have been made. It has, however, been established that tall and short people respectively marry one another more seldom than might be expected at random crossings, since a tall and a short person together make a slightly comical contrast (*Pearson* and *Lee*, 1903). In other words, there is a certain resistance to marriage between tall and short individuals. We have furthermore reason for saying that deaf-mutes relatively often marry deaf-mutes. The affliction makes contact with healthy persons more difficult, but is a bond of union between those possessing the character. We can suspect musical persons of marrying one another particularly often, and, generally, expect hereditary characters of importance for special interests to make for a certain degree of assortative mating: interests unite people. It is less certain whether we can go so far as to state that intelligent people marry their like more frequently than chance demands.

However, we must take into account not only positive assortative mating, where persons with the same characters prefer one another; the possibility of negative assortative mating, where there is a resistance to marriage between persons with the same characters, is also conceivable. For example, it is possible that extremely obstinate or temperamental persons fall into conflict with one another relatively easily, and that in so far as such characters are determined by heredity there is negative assortative mating. It is furthermore easy to assume that, as regards certain defects, there should be negative assortative mating to a certain extent. As regards those characters occasioning a certain helplessness (hereditary blindness, lameness), the actual helplessness may constitute an obstacle to marriage between persons suffering from the same defect, while marriage with normal individuals, on the other hand, is not checked to the same extent. Direct investigations showing the occurrence of negative assortative mating have not hitherto been

made, however. As, up till now, there has been no very general interest in problems regarding genetics of population, there are very few empirical investigations to back up an analysis of processes like this.

Now, we can further differentiate between total assortative mating, where character-bearers exclusively marry each other, and where no one possessing the character marries anyone without it, and partial assortative mating. In the latter case, it is only that character-bearers marry one another rather more often than is to expected in panmixia. The effect of total positive assortative mating has been computed by *Robbins* (1918). Recursion formulæ for partial positive assortative mating have been submitted by *Koller* (1938), who has also used them to arrive at limit values. Both these authors use a complicated system of designation. *Koller* has used the assumption that a certain proportion of unions between dominant and recessive character-bearers are not forthcoming. In the following pages formulæ of a simpler form are deduced, and a new startingpoint for the solution of the problem, giving a more general result, has also been used.

The effect of negative assortative mating has not previously been analysed.

Positive total assortative mating.

According to designations used earlier, persons with the composition *RR* will, in positive total assortative mating and monohybrid diallelism, always marry one another. In the first generation we then get the matings given below, and offspring from these crossings. Cf. Table 9.

If we continue in this way, we find after n generations

$$r_n^2 = r^2 + \frac{nr^2 d}{1 + nr} = \frac{(n+1) r^2}{1 + nr} \tag{50}$$

character-bearers of the type *RR*,

$$d_n^2 = d^2 + \frac{nr^2 d}{1 + nr} \tag{51}$$

of the type *DD* and

$$2 r_n d_n = 2rd + \frac{2nr^2 d}{1 + nr} \tag{52}$$

of the type *RD*.

TABLE 9.

Cf. the text.

Composition of marriage	Frequency in the population	Children		
		Frequency of different types		
		RR_n	RD_n	DD_n
RR × RR	$r^4 + 2r^3d + r^2d^2 = r^2 = a$	a		
RR × RD	$4r^3d - 4r^3d = 0$	0	0	
RR × DD	$2r^2d^2 - 2r^2d^2 = 0$		0	
RD × RD	$4r^2d^2 + \frac{4r^2d^2(2r^2d + r^2d^2)}{(2rd + d^2)^2} = \frac{4r^2d}{1+r} = d'$	$\frac{1}{4}d'$	$\frac{1}{2}d'$	$\frac{1}{4}d'$
RD × DD	$4rd^2 + \frac{4rd^2(2r^2d + r^2d^2)}{(2rd + d^2)^2} = \frac{4rd^2}{1+r} = e$		$\frac{1}{2}e$	$\frac{1}{2}e$
DD × DD	$d^4 + \frac{d^4(2r^2d + r^2d^2)}{(2rd + d^2)^2} = \frac{d^2}{1+r} = f$			f
	Total	$RR_n = a + \frac{1}{4}d' = r^2 + \frac{r^2d}{1+r}$	$RD_n = \frac{1}{2}d' + \frac{1}{2}e = 2rd - \frac{2r^2d}{1+r}$	$DD_n = \frac{1}{4}d' + \frac{1}{2}e + f = d^2 + \frac{r^2d}{1+r}$

In the next generation, i.e. the generation $n + 1$, we then get the following probability for character-bearers of the type *RR:*

$$r^2_{n+1} = \frac{(n+2)\, r^2}{1 + (n+1)\, r}.$$

The validity of this formula is shown thus: In the n^{th} generation the proportion of the recessive gene among the heterozygotes and the dominant homozygotes in the population is:

$$\frac{\left[r - \frac{(n+1)\, r^2}{1+nr}\right]^2}{1 - \frac{(n+1)\, r^2}{1+nr}}.$$

The character-bearers in the n^{th} generation marry each other exclusively, and give in the $(n+1)^{th}$ generation the same proportion of character-bearers as they themselves constituted in the n^{th}. To these bearers, however, are added others derived from random crossings between non-character-bearers. These latter crossings yield a number of character-bearers which is given by the formula below.

$$\frac{\left[r - \frac{(n+1) r^2}{1+nr}\right]^2}{1 - \frac{(n+1)\, r^2}{1+nr}} = \frac{r^2\,(1-r)}{[1 + nr - (n+1)\, r^2]\,[1+nr]}.$$

In all, then, we get in the $(n+1)^{th}$ generation the following number of character-bearers:

$$r^2_{n+1} = \frac{(n+1)\, r^2}{1+nr} + \frac{r^2\,(1-r)}{[1+nr-(n+1)\, r^2]\;[1+nr]} = \frac{(n+2)\;r^2}{1+(n+1)\;r}.$$

This shows that if the formula holds for n generations, it also holds for $(n+1)$ generations. It is easy to show that the formula holds for the 1^{st} generation.

The limit value is obtained by inserting $n = \infty$. We then find that the heterozygotes disappear and that the population comes to consist

of persons of the type *RR*, with the frequency *r*, and persons of the type *DD*, with the frequency *d*. We get an idea of the swiftness of the process from Figs. 16 and 17 and Table 10.

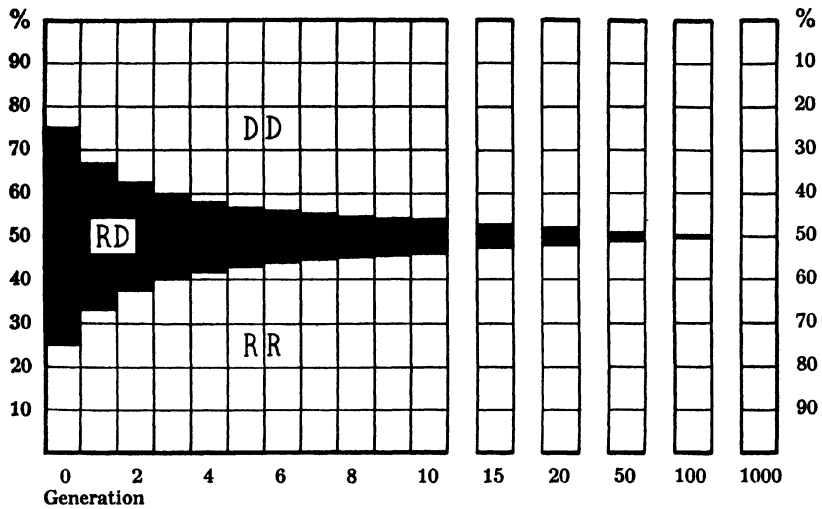


Fig. 16. Frequency of heterozygotes at total, positive assortative mating in successive generations when a recessive gene has the frequency $r = 0.5$. Cf. Table 10.

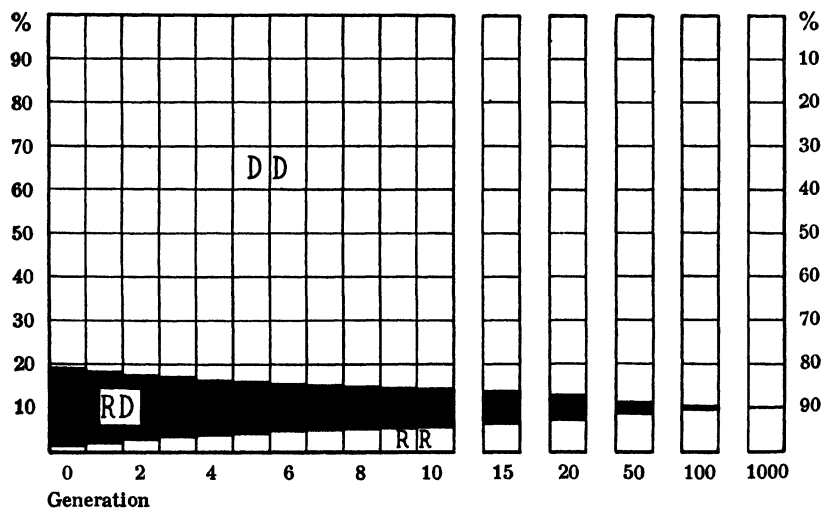


Fig. 17. Frequency of heterozygotes at total, positive assortative mating in successive generations when a recessive gene has the frequency $r = 0.1$. Cf. Table 10.

TABLE 10.

Effect of positive, total assortative mating in successive generations in monohybrid, recessive diallelism when the frequency of character-bearers is varying. Cf. formulæ 50, 51 and 52.

Generation	$r^2 = 0.01\%$			$r^2 = 1\%$			$r^2 = 4\%$			$r^2 = 25\%$		
	RR	RD	DD	RR	RD	DD	RR	RD	DD	RR	RD	DD
0	0.01	1.98	98.01	1.0	18.0	81.0	4.0	32.0	64.0	25.0	50.0	25.0
1	0.02	1.96	98.02	1.8	16.4	81.8	6.7	26.7	66.7	33.3	33.3	33.3
2	0.03	1.94	98.03	2.5	15.0	82.5	8.6	22.9	68.6	37.5	25.0	37.5
3	0.04	1.92	98.04	3.1	13.8	83.1	10.0	20.0	70.0	40.0	20.0	40.0
4	0.05	1.90	98.05	3.6	12.9	83.6	11.1	17.8	71.1	41.7	16.7	41.7
5	0.06	1.88	98.06	4.0	12.0	84.0	12.0	16.0	72.0	42.9	14.3	42.9
6	0.07	1.86	98.07	4.4	11.2	84.4	12.7	14.5	72.7	43.8	12.5	43.8
7	0.07	1.86	98.07	4.7	10.6	84.7	13.3	13.3	73.3	44.4	11.1	44.4
8	0.08	1.84	98.08	5.0	10.0	85.0	13.9	12.3	73.9	45.0	10.0	45.0
9	0.09	1.82	98.09	5.3	9.5	85.3	14.3	11.4	74.3	45.5	9.1	45.5
10	0.10	1.80	98.10	5.5	9.0	85.5	14.7	10.7	74.7	45.8	8.3	45.8
15	0.14	1.72	98.14	6.4	7.2	86.4	16.0	8.0	76.0	47.1	5.9	47.1
20	0.18	1.64	98.18	7.0	6.0	87.0	16.8	6.4	76.8	47.7	4.5	47.7
50	0.34	1.32	98.34	8.5	3.0	88.5	18.6	2.9	78.6	49.0	2.0	49.0
100	0.51	0.98	98.51	9.2	1.6	89.2	19.2	1.5	79.2	49.5	1.0	49.5
1000	0.91	0.18	98.91	9.9	0.2	89.9	19.9	0.2	79.9	50.0	0	50.0
Limit value	1.00		99.00	10.0		90.0	20.0		80.0	50.0		50.0

Now, total assortative mating can hardly be found in human populations. The problem has practical interest for the breeding of animals, and it was from this viewpoint that the problem was originally dealt with by *Robbins*, on the basis of certain crossing schemes submitted by *Jennings*, 1916 and 1917.

Positive partial assortative mating.

As regards human beings, we have only to take into account partial assortative mating, i.e. the crossing of certain character-bearers with one another to a rather greater extent than in panmixia. The process should in principle have the same trend as total assortative mating, i.e. it should make for an increase of the homozygotes at the expense of the frequency of the heterozygotes. We ask ourselves how quickly

a process of this kind advances, and towards what limit value? Does this process, too, advance towards pure homozygosis? A difficulty in solving this problem is that if we assume character-bearers to prefer one another to a certain frequency, which frequency is greater than the one to be expected in panmixia, then the frequency of homozygotes is hereby raised. But when their frequency has become higher, it is difficult to determine what an "unchanged tendency" is to be assumed to imply in the changed situation. Having no experience to back up the assumption, all we can do is to content ourselves with such solutions as seem reasonable—although we do not venture to assert that they with certainty agree with the actual state of affairs in human populations. The assumption most readily presenting itself is that there is a constant resistance to unions between character-bearers of opposite type. A constant proportion of the unions between character-bearers and non-character-bearers, to be expected in random crossings in each generation, is not forthcoming, and the bearers who do not marry one another marry those of the same type. Now, if we assume panmixia and take it that $2k$ of the marriages between character-bearers and non-character-bearers are not contracted, the process will make for a decrease of the frequency of heterozygotes, and the genes of opposed kind, thus prevented from coming together, form homozygotes. If we assume that in a certain generation the decrease of heterozygotes is $2\Delta_n$, each of the homozygote types must have increased by Δ_n. We can now calculate the change taking place from this generation to the next one, and thus arrive at a recursion formula making possible a computation of successive terms. If the generation we started with consists of RR types, with the frequency $r^2 + \Delta_n$, RD individuals with the frequency $2rd - 2\Delta_n$, and DD individuals with the frequency $d^2 + \Delta_n$, we get the frequency of crossings and offspring which is given in Table 11.

The recursion formulæ will then be as follows:

$$RR_n = r^2 + \frac{2kd^2\, RR_{n-1}}{1 - RR_{n-1}}, \tag{53}$$

$$RD_n = 2rd - \frac{4kd^2\, RR_{n-1}}{1 - RR_{n-1}}, \tag{54}$$

$$DD_n = d^2 + \frac{2kd^2\, RR_{n-1}}{1 - RR_{n-1}}. \tag{55}$$

TABLE 11.

Cf. the text.

Composition of marriage	Frequency in the population	Children: Frequency of the types RR_n	Children: Frequency of the types RD_n	Children: Frequency of the types DD_n
$RR_{n-1} \times RR_{n-1}$	$(r^2+\Delta)^2 + k2(r^2+\Delta)(2rd-2\Delta) + k2(r^2+\Delta)(d^2+\Delta) = a$	a		
$RR_{n-1} \times RD_{n-1}$	$2(r^2+\Delta)(2rd-2\Delta) - 2k2(r^2+\Delta)(2rd-2\Delta) = b$	$\frac{1}{2}b$	$\frac{1}{2}b$	
$RR_{n-1} \times DD_{n-1}$	$2(r^2+\Delta)(d^2+\Delta) - 2k2(r^2+\Delta)(d^2+\Delta) = c$		c	
$RD_{n-1} \times RD_{n-1}$	$(2rd-2\Delta)^2 + \frac{2k[(r^2+\Delta)(2rd-2\Delta)+(r^2+\Delta)(d^2+\Delta)][2rd-2\Delta]^2}{[(2rd-2\Delta)+(d^2+\Delta)]^2} = d'$	$\frac{1}{4}d'$	$\frac{1}{2}d'$	$\frac{1}{4}d'$
$RD_{n-1} \times DD_{n-1}$	$2(2rd-2\Delta)(d^2+\Delta) + \frac{2k[(r^2+\Delta)(2rd-2\Delta)+(r^2+\Delta)(d^2+\Delta)][2(2rd-2\Delta)(d^2+\Delta)]}{[(2rd-2\Delta)+(d^2+\Delta)]^2} = e$		$\frac{1}{2}e$	$\frac{1}{2}e$
$DD_{n-1} \times DD_{n-1}$	$(d^2+\Delta)^2 + \frac{2k[(r^2+\Delta)(2rd-2\Delta)+(r^2+\Delta)(d^2+\Delta)][d^2+\Delta]^2}{[(2rd-2\Delta)+(d^2+\Delta)]^2} = f$			f
	Total	$RR_n = a + \frac{1}{2}b + \frac{1}{4}d' = r^2 + \frac{2kd^2(r^2+\Delta)}{1-(r^2+\Delta)}$	$RD_n = \frac{1}{2}b + c + \frac{1}{2}d' + \frac{1}{2}e = 2rd - \frac{4kd^2(r^2+\Delta)}{1-(r^2+\Delta)}$	$DD_n = \frac{1}{4}d' + \frac{1}{2}e + f = d^2 + \frac{2kd^2(r^2+\Delta)}{1-(r^2+\Delta)}$

The limit value for the series can be reached as follows. We assume panmixia and calculate the successive changes during a number of generations. We further assume a population in which total assortative mating has taken place for so long that heterozygotes have completely disappeared. If, with this starting-point, we calculate the effect of partial assortative mating with the help of the recursion formula given above, we get a successive increase of heterozygosis and decrease of homozygosis. We now find that, after only a moderate number of generations, the values obtained on the assumption of panmixia, and proceeding from the limit value for total assortative mating at a certain gene frequency, lie very close to one another. The limit value of the process must lie between the two values, and after 6—7 generations this value has been so narrowed down that no more exact idea of it is required in practice.

Figures 18 and 19 and Table 12 indicate the course of the process, and the limit values. It is seen that even a very powerful assortative mating has a moderate effect. The effect is greater on rare characters than on more common ones. But even if we assume a very marked assortative mating for a rare character, the decrease of the heterozygotes and the increase of the homozygotes will not be very great.

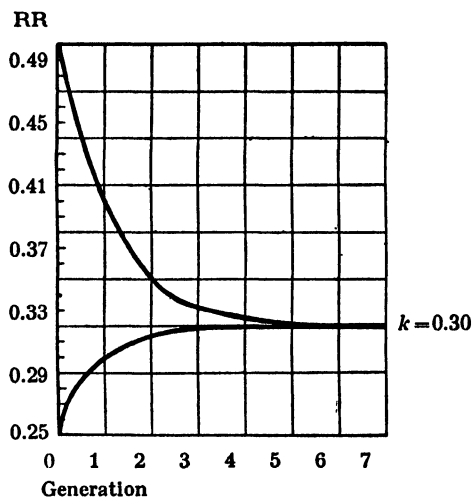


Fig. 18. Effect of positive, partial assortative mating in successive generations with the intensity $k = 0.30$, when the frequency of the recessive gene is $r = 0.5$. (Cf. Table 12.) In the calculations we have started from panmixia and also assumed that because of total assortative mating at the start there are no heterozygotes in the population.

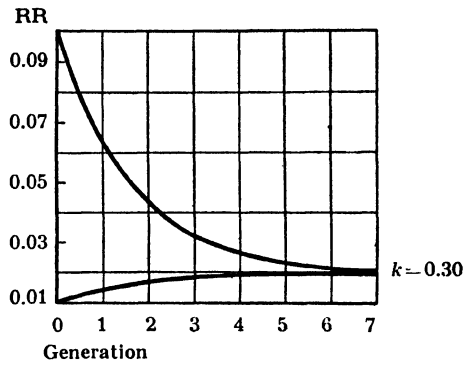


Fig. 19. Effect of positive, partial assortative mating in successive generations with the intensity $k = 0.30$, when the frequency of the recessive gene is $r = 0.1$. (Cf. Table 12.) In the calculations we have started from panmixia and also assumed that because of total assortative mating at the start there are no heterozygotes in the population.

TABLE 12.

Effect of different intensity (k) of positive, partial assortative mating in successive generations and in monohybrid, recessive diallelism when the frequency of recessive character-bearers is varying. Cf. formula 53.

Generation	$r^2 = 0.001$		$r^2 = 0.01$		$r^2 = 0.25$	
	$k = 0.10$	$k = 0.30$	$k = 0.10$	$k = 0.30$	$k = 0.10$	$k = 0.30$
0	0.00100	0.00100	0.0100	0.0100	0.2500	0.2500
1	0.00119	0.00156	0.0116	0.0149	0.2667	0.3000
2	0.00122	0.00188	0.0119	0.0174	0.2682	0.3143
3	0.00123	0.00206	0.0120	0.0186	0.2683	0.3188
4		0.00216		0.0192		0.3202
5		0.00222		0.0195		0.3207
6		0.00225		0.0197		0.3208
7		0.00227		0.0198		0.3209
8		0.00228				

Let us say that a character has a frequency of 1 %, for example; the increase, if 60 % of the marriages between character-bearers and non-character-bearers are not contracted will all the same not be more than about 98 %. That is to say, the number of bearers is not quite doubled. The heterozygotes drop from 18 % to 16.14 %. For a still rarer character, with a frequency of 0.1 %, for example, the final result will be a frequency of the character-bearers of 0.12 %, when 20 % of the marriages between character-bearers are prevented.

Another way of solving the problem is to assume that unions between character-bearers are contracted in a constant proportion, h, of the number we would get in each generation if these unions were contracted at random. It is difficult to determine whether an assumption like this is reasonable; we have maintained above that it is by no means to be regarded as self-evident. If, however, this assumption is made, we get the unions and offspring given in Table 13.

The recursion formula obtained is as follows:

$$RR_{n+1} = RR_n h + \frac{2\,RR_n\,(r - RR_n)\,(1-h)}{1-RR_n} + \\ + \frac{(r-RR_n)^2\left[1 - \dfrac{RR_n\,(1-h)}{1-RR_n}\right]}{1-RR_n}. \qquad (56)$$

If $h = r^2$, there is no change. The composition of the population will be constant—the same as in panmixia. If h is greater than this value, then we have positive assortative mating. If we put $h = 1$, we get total assortative mating and the same formula as before for this process. (If h is less than r^2, we have negative assortative mating.) It should be remembered that h does not mean the same as k did in the formulæ obtained earlier on. Now it is assumed that a certain constant proportion of the recessive homozygotes contract marriage—in the earlier formulæ it was assumed that a constant proportion of the expected marriages between heterozygotes were not contracted.

Negative total and partial assortative mating.

The effect of negative assortative mating has not previously been worked out. As has been maintained above, it is not established whether there be such a process in human populations, though it is certainly not inconceivable. We now find that the same formulæ hold for a process of this kind as for positive partial assortative mating. If we assume that marriages between heterozygotes increase by a certain proportion, k, then the sign between the terms is changed in the recursion formula, which thus becomes:

$$RR_{n+1} = r^2 - \frac{2kd^2\,RR_n}{1-RR_n}. \qquad (57)$$

TABLE 13.

Cf. the text.

Composition of marriage	Frequency in the population	Children		
		Frequency of the types		
		RR_n	RD_n	DD_n
$RR_{n-1} \times RR_{n-1}$	$(r^2+\Delta)h = a$	a		
$RR_{n-1} \times RD_{n-1}$	$\frac{2(r^2+\Delta)(2rd-2\Delta)(1-h)}{1-(r^2+\Delta)} = b$	$\frac{1}{2}b$	$\frac{1}{2}b$	
$RR_{n-1} \times DD_{n-1}$	$\frac{2(r^2+\Delta)(d^2+\Delta)(1-h)}{1-(r^2+\Delta)} = c$		c	
$RD_{n-1} \times RD_{n-1}$	$\frac{(2rd-2\Delta)^2\left[1-\frac{(r^2+\Delta)(1-h)}{1-(r^2+\Delta)}\right]}{\left[1-\frac{(r^2+\Delta)(1-h)}{1-(r^2+\Delta)}\right][1-(r^2+\Delta)]} = d'$	$\frac{1}{4}d'$	$\frac{1}{2}d'$	$\frac{1}{4}d'$
$RD_{n-1} \times DD_{n-1}$	$\frac{2(2rd-2\Delta)(d^2+\Delta)\left[1-\frac{(r^2+\Delta)(1-h)}{1-(r^2+\Delta)}\right]}{1-(r^2+\Delta)} = e$		$\frac{1}{2}e$	$\frac{1}{2}e$
$DD_{n-1} \times DD_{n-1}$	$\frac{(d^2+\Delta)^2\left[1-\frac{(r^2+\Delta)(1-h)}{1-(r^2+\Delta)}\right]}{1-(r^2+\Delta)} = f$			f
	Total	$RR_n = a+\frac{1}{2}b+\frac{1}{4}d'$	$RD_n = \frac{1}{2}b+c+\frac{1}{2}d'+\frac{1}{2}e$	$DD_n = \frac{1}{4}d'+\frac{1}{2}e+f$

If, on the other hand, we assume that a certain constant proportion of the recessive homozygotes, i.e. h (less than r^2), do not marry one another, then the recursion formula (56) given earlier on holds.

$$RR_{n+1} = RR_n h + \frac{2\,RR_n\,(r - RR_n)\,(1-h)}{1-RR_n} + \\ + \frac{(r-RR_n)^2\left[1 - \frac{RR_n(1-h)}{1-RR_n}\right]}{1-RR_n}.$$

If we want to use these formulæ to get the values for negative total assortative mating, we can put $h = 0$ in the latter one. On the other hand, we cannot put $k = 1$ in the first, as this implies that marriages between persons with opposed characters would in certain cases increase by a greater proportion than is possible in respect of the frequency of character-bearers. In negative total assortative mating the limit value will be:

$$k = \frac{RR_{n-1}}{2\,(1 - RR_{n-1})}. \tag{58}$$

If this expression is inserted in the first formula, and if we put $h = 0$ in the second, we get the following expression for the relation between two consecutive terms:

$$RR_{n+1} = r^2 - \frac{d^2\,RR_n^2}{(1 - RR_n)^2}. \tag{59}$$

The values in diagram 20 and Table 14 have been calculated with the help of these formulæ. The heterozygotes are found to increase during a moderate number of generations, and the series to oscillate towards a limit value. The reason for this is that, if negative assortative mating is introduced in panmixia, the heterozygotes are considerably increased in the first generation. This means that the next generation is fairly extensively recruited from marriage between heterozygotes. From these marriages, however, spring relatively many homozygotes, so that their frequency in the third generation will be greater than it was in the second. After a comparatively small number of generations,

however, a state of balance is reached, which nevertheless diverges to a moderate extent from panmixia. If, for example, $r = \frac{1}{2}$, and there are thus recessive character-bearers in 25 % of the population, total negative assortative mating brings about a change after 3—4 generations to a fairly stable state of 22.8 %.

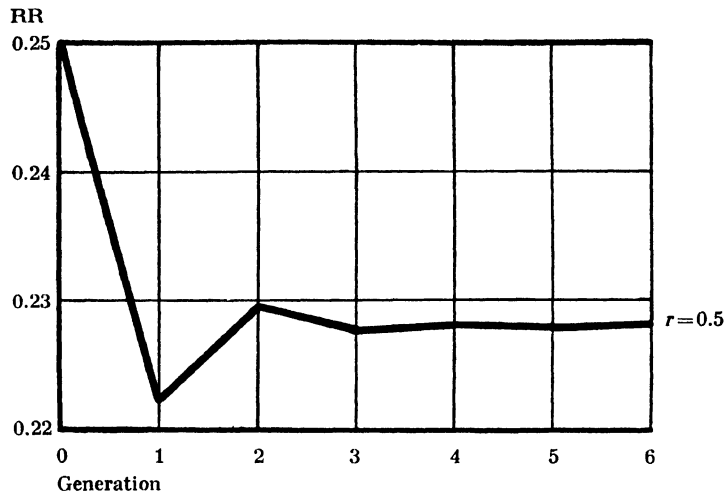


Fig. 20. Total, negative assortative mating in successive generations when the recessive gene has the frequency $r = 0.5$. Cf. Table 14.

TABLE 14.

Total, negative assortative mating in successive generations in recessive, monohybrid diallelism, when the frequency of character-bearers is varying. Cf. formula 59.

Generation	$r^2 = 0.001$	$r^2 = 0.01$	$r^2 = 0.1$	$r^2 = 0.25$
0	0.001000	0.01000	0.10000	0.2500
1	0.000999	0.00992	0.09423	0.2222
2		0.00999	0.09494	0.2296
3			0.09486	0.2278
4			0.09487	0.2282
5			0.09486	0.2281
6				0.2282

Assortative mating, inmarriage, selection, and mutation.

In principle, positive assortative mating has a similar effect to inmarriage, i.e. it sets up an increase of homozygosis at the expense of heterozygosis. Other things being equal, the effect is in both processes stronger on rare characters than on common ones. It must, however, be remembered that assortative mating can hardly be thought to play any very great part for very rare characters, since the bearers will not then have any appreciable prospects of meeting one another. It is scarcely likely, therefore, that assortative mating should play any great part in human populations, and the deviation from panmixia which it, together with inmarriage, occasions can doubtless be more or less disregarded in most cases. Nor is it likely, then, that these processes would particularly influence the heterozygous frequency in the state of balance obtaining in a given situation between mutations and selection. (Nevertheless, owing to the development of communications, moving in to towns, etc., there is reason to suppose that the balance has been upset, and that assortative mating plays a rather greater part nowadays in civilized communities than earlier on.) At present, however, it is not possible to reach definitive numerical gauges of the importance of these different processes when they move along at the same time, as we have no experience to back up the calculations. This problem will be discussed more thoroughly in a following chapter.

The importance of the isolate for the composition of populations.

When drawing up formulæ in the previous pages, we have started from a population with panmixia, but we have not discussed the conception of population in more detail. Strictly speaking, a population is in this connexion the number of people among whom panmixia prevails. In practice, we can of course establish with certainty that panmixia

never obtains beyond the political boundaries of a country. A more natural assumption seems to be that panmixia obtains within a nation. It is nevertheless clear that this assumption is not justified, particularly if a large nation is in question. An individual living in a certain part of a country has the possibility of marrying within a certain limited area of that country, and within a certain social stratum. A nation, a great population, consists then of partial populations – minor units within which we have a greater right to assume panmixia. The partial populations thus constituting a large nation are called isolates. The boundaries in question here are partly of a geographical kind, e.g. woods and water-courses, and partly of a social kind. An individual in a certain class of society does not have much possibility of marrying above or beneath the class to which he belongs.

The size of the isolates.

It is now of a certain interest to get an idea of the size of the isolates. As *Dahlberg* showed (1929), this can be done with the help of the inmarriage frequency. We have already maintained that, in panmixia, consanguineous marriages must take place at random. The frequency of these marriages will naturally depend partly on the size of the population, and partly on that of the siblings. Let us assume that b is the average number of children who become adult and marry in each sibling-group, and that n is the number of individuals of this kind in the entire population.

If we now select an individual at random from the population, he will have on an average b (b—1) cousins to whom he can get married. The total number of individuals to whom he can get married is $\frac{n}{2}$. The probability for a cousin marriage c is thus:

$$c = \frac{2b\,(b-1)}{n} \text{ and } n = \frac{2b\,(b-1)}{c}. \qquad (60)$$

When drawing up this formula it was not necessary to take into account differences of sex since an individual cannot marry another of the same sex. This factor exerts the same check on marriage between relations as on that between non-related individuals in the

population. As regards the difference of age between members of a population, we might venture to say that this is greater rather for the total number of individuals than for cousins. If, in other words, we take two cousins at random, the probable difference in their ages is less than that between two non-related individuals similarly selected. This means that the actual frequency figure for marriages between cousins should be somewhat greater than the formula indicates. At present it is hardly possible to gauge the importance of these factors exactly. Nevertheless, it is *a priori* hardly likely that they should have any great importance; we can no doubt thus assume that the frequency figure for marriages between cousins, which we find empirically, corresponds more or less to what the formula would lead us to expect—at any rate in a number of populations. The number of children per marriage in Western Europe is approximately two. It may be remembered that the question is one of adult children, contracting marriages. If this number is, on an average, two per family, the population remains constant. If the number is three, the population increases by 50 % in one generation. As the populations are fairly constant as to size, this means that the number of children is approximately two. If the number of children is set at two, we find in different frequencies of marriages between cousins the values given in Table 15. It should, however, be remembered that these values

TABLE 15.

Size of the isolates ($= n$), when marriages between cousins are contracted at random in different frequencies ($= c$). Cf. formula 60.

c	n
0.0001	40 000
0.001	4 000
0.0025	1 600
0.005	800
0.01	400
0.05	80
0.1	40

are approximate. We have assumed that the size of the family is constant, or varies only slightly. If the variation is more considerable, this must mean we have to expect a higher frequency of marriages

between cousins; this in its turn means that the figures given in the table are, throughout, rather too low. However, it would hardly be of any interest to make more correct calculations, since we are only concerned with getting an idea of the size of the isolates. It must be stated in this connexion that the isolate conception used here idealizes the situation. Strictly speaking, the isolates for two individuals never coincide exactly, and the isolate for certain persons merges gradually into the population without it always being possible to speak of sharp boundaries. The greater the distance between two persons of the opposite sex is, the smaller are their prospects of marrying one another. When the distance exceeds a certain limit, there is, practically speaking, no possibility of these individuals marrying. A group of persons near one another have, on the whole, a common isolate, however. In other words, the differences between the isolates of the different persons are negligible. The conditions are, of course, different in different populations. In some there are sharp isolate boundaries, in others they are less sharp. But in these latter, too, there is, of course, isolation in so far as one person has the opportunity of marrying only a limited number of individuals. It must further be remembered that an isolate is not sharply limited in time. The generations pass into one another without clear dividing-lines. Here, too, we have allowed ourselves to idealize. Like the generations, the isolates we assume are thus fictitious, and are sharply demarcated units, replacing the indeterminate isolates and generations of reality. It is necessary to bear this in mind when using the isolate conception.

When out to get an idea of the size of the isolate, it should first and foremost be remembered that this naturally varies to a high degree. The one extreme is the large town with its never-resting human masses. The other extreme is country of wild, deserted nature, e. g. in Northern Europe, with small isolated villages. As well as this, the size of the isolates is at present undergoing violent changes, on account of the development of communications, emigration to towns, etc. Going on available figures, we can probably assume that in older times the marriages between cousins stood at about 1 %, which corresponds to an isolate of 400 individuals. Nowadays, marriages between cousins seem to approach 0.25 %, which corresponds to an isolate of 1600 individuals. This would mean that, on an average, a person, contracting a marriage has the possibility of choosing from 800 persons nowadays, and from only 200 previously.

Now it is clear that if two isolates effecting exchanges have different compositions, then this exchange must bring about a levelling-out of the difference between them, provided there is no selection in the crossings taking place beyond the isolate boundary. It is obvious that there is greater reason to expect a selection of this kind in respect of social boundaries than in respect of geographical ones. If there is no selection, the crossings beyond the isolate boundary must make for a levelling-out of any possible hereditary difference between the isolates. When this has been done, the boundaries have no importance. We can then take it that panmixia obtains for the whole of the population.

Our next interest is to investigate what the result will be if the isolates differ from one another in composition.

The importance of the isolate boundaries in monohybrid diallelism.

Let us consider a population consisting of two isolates, between which there are crossings. In each isolate there is panmixia. Let us call the isolates G and H, and assume that their size is in the ratio $g : h$, and that $g + h = 1$. The gametes with the recessive gene R have in G the frequency r_g, and in H the frequency r_h. The frequencies of the corresponding dominant gene D are d_g and d_h respectively; $r_g + d_g = 1$, and $r_h + d_h = 1$. The constitution of the isolates is shown in Table 16 (which, together with Table 17, is taken from a work by *Wahlund* [1928]. *Wahlund* was the first who dealt with these problems. We are here following his exposition.)

TABLE 16.

Cf. the text.

Zygotes	Proportions	
	in G	in H
Recessive homozygotes, RR	r_g^2	r_h^2
Heterozygotes, RD	$2r_g d_g$	$2r_h d_h$
Dominant homozygotes, DD	d_g^2	d_h^2
Recessive character-bearers, RR . . .	r_g^2	r_h^2
Dominant character-bearers, RD + DD	$1-r_g^2$	$1-r_h^2$

We get the conditions in the entire population by amalgamating the isolates in proportion to their size. The result is seen in Table 17.

TABLE 17.

Cf. the text.

Zygotes	Proportions in the total population ($G+H$)		
	Observed (1)	Calculated from the proportions of gametes in panmixia (2)	Surplus (1) − (2) = (3)
Recessive homozygotes, RR	$gr_g^2 + hr_h^2$	$(gr_g + hr_h)^2$	$+ gh(r_g - r_h)^2$
Heterozygotes, RD	$2gr_g d_g + 2 \cdot hr_h d_h$	$2(gr_g + hr_h) \cdot (gd_g + hd_h)$	$- 2gh(r_g - r_h)^2$
Dominant homozygotes, DD	$gd_g^2 + hd_h^2$	$(gd_g + hd_h)^2$	$+ gh(r_g - r_h)^2$
Recessive character-bearers, RR	$gr_g^2 + hr_h^2$	$(gr_g + hr_h)^2$	$+ gh(r_g - r_h)^2$
Dominant character-bearers, RD + DD . . .	$1 - gr_g^2 - hr_h^2$	$1 - (gr_g + hr_h)^2$	$- gh(r_g - r_h)^2$

In the total population we thus get more homozygotes (*RR* and *DD* individuals) than we would have done had panmixia obtained in the whole of the population and had there been no isolate boundaries (column 2). The surplus of either kind of homozygote is determined by the positive expression $gh\,(r_g - r_h)^2$. This expression also gives the increase of the recessive character-bearers and double the decrease of the heterozygotes.

Fig. 21 gives the homozygous surplus under different conditions. The difference between the gamete proportions $(r_g - r_h)$ in the isolates is given along the abscissa. The ordinates of the curves give the homozygote increase according to the expression given above.

The greater the differences between the gamete proportions in the two isolates, the greater will the homozygote increase be. The smaller the difference in size between the isolates, the greater the surplus. The maximal effect of the isolates is obtained if they are equally large, and if the difference between the gamete proportions in them is equal to 1. In this case each isolate will consist of the respective kind of homozygotes; there will be no heterozygotes. If the isolates are of the same size, we should get 50 % heterozygotes with this gamete

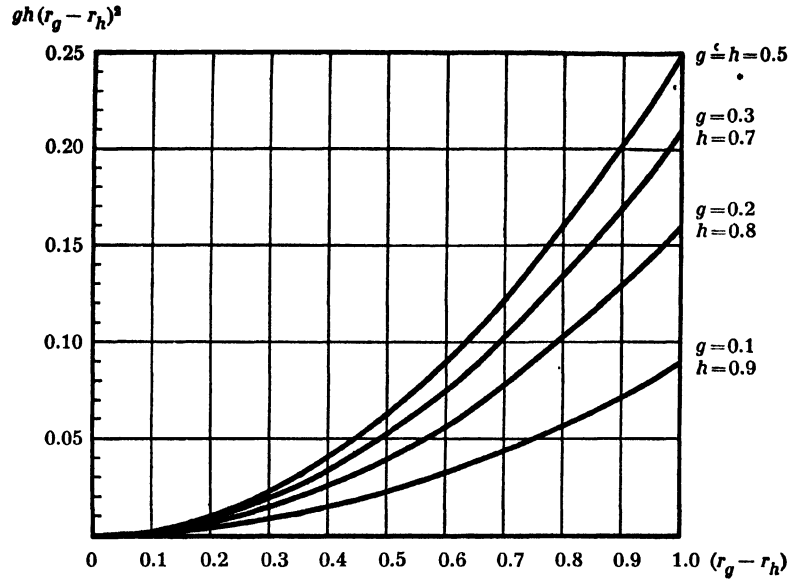


Fig. 21. Difference $gh\ (r_g - r_h)^2$ between the real proportions and those calculated from the gamete proportions calculated ratios of homozygotes RR or DD, when the difference $(r_g - r_h)$ between the gamete frequencies in two isolates of the population and also the respective share in the population of the two isolates, g and h, varies.

composition, and their disappearance is thus the maximal effect the isolates can have. The smaller the one isolate is in relation to the other, and the smaller the difference in their gene composition, the smaller will be the importance of the isolate boundaries.

In an analogous way we can show that, if we have m isolates, which have proportionally the size $i_1 i_2 i_3 \ldots i_m$, with the gene content $r_1 r_2 r_3 \ldots r_m$, and if the frequency of R genes in the whole population is r, the surplus of recessive (or dominant) homozygotes will be:

$$\sigma_i^2 = i_1 (r - r_1)^2 + i_2 (r - r_2)^2 + i_3 (r - r_3)^2 + \ldots + i_m (r - r_m)^2. \quad (61)$$

We will call this expression σ_i^2, for it is the same as the square of the standard deviation for a series composed of the gamete proportions in the different isolates in proportion to the size of the isolates.

This fact has practical interest. Let us say we make an empirical investigation of a certain population, and divide up the investigated material into a number of districts; we should then find a certain

variability in the proportion of recessive monohybrid character-bearers due to a random variation whose extent is determined by the size of the material. We will call the standard deviation derived from this source σ_n. We get, further, a variability determined by a possibly different gene content in the different isolates. We found an expression for this standard deviation above, and we called it σ_l. The composite, empirically discovered standard deviation, σ_e, is thus made up of two kinds of standard deviation according to the formula:

$$\sigma_e = \sqrt{\sigma_n^2 + \sigma_l^2}. \tag{62}$$

The standard deviation to be expected on the basis of the size of the isolates and the average gene content can easily be computed theoretically. As we know σ_n and σ_e, in the equation above, we can by calculation assess the variation due to the isolates.

Now, if the isolates at one's disposal are large, the standard deviation due to their limited size will become extremely small. The empirically found standard deviation will then be due almost entirely to the differences between the isolates of the population. With very extensive material, the standard deviation found in division into minor but not unduly small districts may thus be practically entirely attributed to, and taken as an expression of the homozygote surplus occasioned by the isolate boundaries. If, then, this standard deviation is small or non-existent, the boundaries lack importance; the population is, as regards heredity, homogeneous.

In a population of this kind the frequency of the recessive homozygotes is r^2, of the dominant homozygotes d^2, and of the heterozygotes $2rd$. We can thus calculate r from the frequency of recessive character-bearers. If the isolate boundaries are of consequence, and if the gene content of the isolates therefore differ from one another, a calculation like this gives an incorrect value for the frequency of R gametes. The correct value for their frequency, r_l, is obtained if we call the frequency of the recessive character-bearers r^2 and calculate σ_l^2 in the way given above from the expression:

$$r_l = \sqrt{r^2 + \sigma_l^2}. \tag{63}$$

The corrected value for the frequency of the D genes is obtained from:

$$1 - \sqrt{r^2 + \sigma_l^2}. \tag{64}$$

On the whole, we might well expect the isolate boundaries to be of importance, primarily for rare characters. In questions of ordinary characters (if we except racial differences; cf. below) it is not so likely that there should be differences between isolates so extensive as to cause appreciable divergences from what is to be expected in panmixia throughout the entire population. The very fact that a character is common, i. e. occurs generally, to a certain extent excludes major differences between the isolates of a population. If, on the other hand, a character is rare, it must by virtue of its very rarity be able to occur only in some isolates, while it is absent from others. In a situation like this we must take the isolate boundaries into account if we want to calculate the heterozygous frequency. If, for example, we investigate how a rare disease occurs in a country, and find that it only appears in limited centres, we cannot when calculating the heterozygous frequency postulate panmixia throughout the whole of the population: this would plainly give us far too high a value. We must confine the calculation to the isolates where the disease occurs (and a corresponding number of isolates without the character): this will yield a considerably lower heterozygous frequency for the whole country than is obtained after the erroneous method of calculation. (*Sjögren*, 1931, for example, has computed the heterozygous frequency for juvenile amaurotic idiocy in Sweden at 1 %. The correct figure is a fraction of this.)

One reason why the isolate boundaries are of interest is that they explain why we find serious, rare recessive diseases in remote demarcated districts. To understand this we have only to remember that when a mutation appears in a population in a certain isolate and spreads inside (but hardly outside) this isolate the probability of the gene meeting in a double dose is greater if the isolate is small than if it is large. The conditions in a little, remote village, with poor communications, are favourable for the appearance of diseases of this kind. In large isolates, e. g. in a metropolis, the chance of such a gene's manifesting itself is, on the other hand, slight. It is for this reason that we find serious nervous diseases, forms of idiocy, and the like, in districts situated far from the madding crowd where the communications are poor. In these districts the mode of life is as a rule rather primitive and the population seems to be on a low cultural level. We are therefore very inclined to associate the hereditary disease with the primitive culture, and imply more or less definitely that

both phenomena are due to a degeneration with its roots in inmarriage. In point of fact it is the lack of communications that is the cause, since the isolate boundary is thereby maintained. The cultural level is naturally of no consequence from the point of view of heredity. Inmarriage can, of course, be said to play a part, but this inmarriage need only be what we have to expect in panmixia within the isolate.

Isolate-breaking in monohybridism.

These considerations lead us on to the question of how important the breaking of isolate boundaries may be. We will first investigate the importance of isolate-breaking in monohybrid diallelism, assuming we are dealing with a rare gene, not found in the surrounding isolates. (Cf. *Dahlberg*, 1938.) If the frequency of the gene is r, and the isolate increases by a part of itself, a, the gene frequency in the new isolate will be $\frac{r}{1+a}$ and the frequency of the character-bearers:

$$RR = \frac{r^2}{(1+a)^2}$$

If, in other words, an isolate is doubled, the frequency of the character-bearers will drop to $\frac{1}{4}$ of the original frequency. If, however, the frequency of the character-bearers is diminished in this way, it must be remembered from the point of view of the population that the size of the isolate has increased to $1+a$. The lower frequency thus applies to this increased isolate, so that as regards the population the frequency of the character-bearers decreases according to the formula:

$$RR = \frac{r^2}{1+a}. \tag{65}$$

This means that the frequency of the character-bearers in a population decreases in proportion to the isolate-breaking there. If the isolate is doubled, the character-bearers drop to half. In other words, a process of very crucial importance is at present going on as regards the frequency of monohybrid recessive defects. Industrialisation, the develop-

ment of communications, and the moving in to the towns mean that the isolates are broken; one of the things showing this is a decrease in the frequency of marriages between cousins, as has already been pointed out. However, this decrease is due in part to the increase of the population. When a people increases in number, then the separate isolates must needs also increase. The increase due to an isolate growing within itself has no effect on the frequency of the genes within the isolate, unless selection or mutations cause changes here. Even if we take it that part of the decreased frequency of marriages between cousins is due to a population increase, a considerable part of it must be due to isolate-breaking. If we want to be cautious, we can reckon on the isolate's being at least doubled, and perhaps trebled, to judge from figures for the frequency of cousin marriages in certain parts of Germany. This should have meant that the frequency of rare monohybrid recessive defects dropped to round about a half or a third. (The fact that the frequency of defective individuals has increased in official statistics is probably connected with a better system of registration.)

It may finally be stated that the difference between town and country as regards the frequency of defective individuals is partly determined by the fact that those who have emigrated to the towns constitute a selected material, among which the defective are underrepresented. There is no doubt, however, that this difference is partly due to the fact that the towns are major isolates, in which the genes only appear in heterozygotes, thus having small chance to meet in homozygous form.

We have investigated the breaking of isolates on the assumption that we are dealing with very rare genes, only occurring in a minor number of the isolates in a population; at the same time we assumed that the isolates increase in size on account of isolate-breaking. We can go a step further and investigate the effect of an isolate-breaking when there are only differences in gene frequency between the different isolates. (Cf. *Wahlund*, 1928.) For the sake of simplicity we will assume that an exchange takes place between the isolates without their changing the proportion of the population they constitute. In a constant population, then, the isolates are assumed to be constant; this means that an immigration into a given isolate is accompanied by an emigration of the same extent. Let us assume that in a given isolate the gene has the frequency r_{s_1} and that a certain part of the isolate, a, consists of immigrants who are exchanged for emigrants. The immigrants

have the gene proportion r_{x_1}. We then get the following proportion of the gene:

$$r_{s_1} = (1 - a_{s_1})\, r_s + a_{s_1}\, r_{x_1}.$$

In the next generation we get the proportion:

$$r_{s_2} = (1 - a_{s_2})\, r_{s_1} + a_{s_2}\, r_{x_2},$$

and after n generations:

$$r_{s_n} = (1 - a_{s_n})\, r_{s_{(n-1)}} + a_{s_n}\, r_{x_n}. \tag{66}$$

If the immigrants have a constant gene content, r_x, after n generations the difference between the gene content of the isolate and that of the immigrants will be:

$$r_{s_n} - r_x = (1 - a_{s_n})\, (r^s_{(n-1)} - r_x).$$

The total change will then be:

$$r_{s_n} - r_x = (1 - a_{s_1})\, (1 - a_{s_2})\, (1 - a_{s_3}) \ldots (1 - a_{s_n})\, (r_s - r_x);$$

and if we put:

$$1 - a_s = \sqrt[n]{(1 - a_{s_1})\, (1 - a_{s_2})\, (1 - a_{s_3}) \ldots (1 - a_{s_n})},$$

we get the following formula:

$$r_{s_n} - r_x = (1 - a_s)^n\, (r_s - r_x). \tag{67}$$

As a_s is a proper fraction, $(1 - a_s)^n$ gets nearer and nearer the value 0 as n increases; this means that the difference in gene content between the immigrants and the isolate gradually disappears and that the change at first proceeds quickly, and then more slowly.

We can now replace an immigration, of varying magnitude and with varying content, from a population into an isolate, by an immigration of varying magnitude but constant content, corresponding to that of the population. In so doing we must correct in respect of the proportion of the population which the isolate constitutes. In

a particular isolate, e. g. the s^{th}, whose proportion of the total population is assumed to be i_s and whose original recessive gamete population is given by r_s, it can easily be shown that the first immigration will have the following gene content:

$$r_{s_1} = \frac{1}{1-i_s} r - \frac{i_s}{1-i_s} r_s.$$

The proportion in the second immigration will have the following character:

$$r_{s_2} = \frac{1}{1-i_s} r - \frac{i_s}{1-i_s} r_{s_1}$$

and so on. It is assumed, that is to say, a levelling-out process takes place; further, that in each isolate the immigration consists of a representative selection from the other isolates. For

$$a_{s_1},\ a_{s_2},\ a_{s_3},\ \ldots\ a_{s_n}$$

we can substitute

$$\frac{a_{s_1}}{1-i_s},\ \frac{a_{s_2}}{1-i_s},\ \frac{a_{s_3}}{1-i_s},\ \ldots \frac{a_{s_n}}{1-i_s}.$$

This gives us the following equation:

$$r_{s_n} - r = \left(1 - \frac{a_{s_1}}{1-i_s}\right)\left(1 - \frac{a_{s_2}}{1-i_s}\right)\left(1 - \frac{a_{s_3}}{1-i_s}\right)\ldots$$
$$\ldots\left(1 - \frac{a_{s_n}}{1-i_s}\right)(r_s - r).$$

If $\frac{a_s}{1-i_s}$ is put $= b_s$ and if

$$1 - b_s = \sqrt[n]{(1-b_{s_1})(1-b_{s_2})(1-b_{s_3})\ldots(1-b_{s_n})},$$

we get:

$$r_{s_n} - r = (1-b_s)^n (r_s - r). \tag{68}$$

If the immigration and emigration constitute a proportion, p_s, of the population, then

$$a_s = \frac{p_s}{i_s} \quad \therefore b_s = \frac{p_s}{i_s(1-i_s)}.$$

In panmixia the probability of a crossing between the isolates and the rest of the population is $2i_s(1-i_s)$. As we assumed that emigration and immigration are equal, half of the marriages will take place within the isolate and half in the population. In panmixia, then, the proportion of immigrants and emigrants is $i_s(1-i_s)$. The real proportion is p, and the expression therefore shows that b_s is the proportion which the immigrants constitute of that immigration we would get in panmixia. If there is no immigration, $b_s = 0$. And in panmixia $b_s = 1$. If the divergence from 1 is called β_s, so that $\beta_s = 1 - b_s$, we get a direct measure of the strength of the isolation. Thus β_s is a measure of the isolation, an *isolation factor*. We can thus write the formula:

$$r_{s_n} - r = (\beta_s)^n (r_s - r). \tag{69}$$

Analogous formulæ can be drawn up for other isolates; we therefore get the following expression for the isolates' divergence from the gene content of the population after n immigrations:

$$\sigma_n^2 = r_1(\beta_1)^{2n}(r_1 - r)^2 + r_2(\beta_2)^{2n}(r_2 - r)^2 + \cdots + r_s(\beta_s)^{2n}(r_s - r)^2. \tag{70}$$

If we replace the isolation factors $\beta_1, \beta_2 \ldots \beta_s$ by an average factor β, we get the following formula:

$$\sigma_n^2 = (\beta)^{2n}\sigma^2 \tag{71}$$

or

$$\sigma_n = (\beta)^n \sigma.$$

From this we get:

$$n = \frac{\log \frac{\sigma_n}{\sigma}}{\log \beta}. \tag{72}$$

With the help of this formula we can calculate how many generations must pass at a certain intensity of the isolation before a certain degree of levelling-out has taken place between the isolates. For example, we can demand that the levelling-out should involve a decrease of the standard deviation to $\frac{1}{10}$ or $\frac{1}{20}$. It is found that if the isolation factor is 0.5, a homogeneity of the population has been reached after 3 generations, which means that the standard deviation has decreased to $\frac{1}{10}$. After 4 generations the standard deviation is $\frac{1}{20}$. If the isolation factor is 0.9, the corresponding figures are 22 and 29 generations. Cf. Table 18.

TABLE 18.

Rapidity of the levelling-out of the gamete proportions in a population at different values of the isolation factor.

In a population regarded as homogeneous, when the standard deviation is decreased to	homogeneity is reached after the following number of generations, if the isolation factor is =								
	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
$\frac{1}{5}$	1	1	1	2	2	3	5	7	15
$\frac{1}{10}$	1	1	2	3	3	5	6	10	22
$\frac{1}{20}$	1	2	3	3	4	6	8	13	29

The breaking up of isolates in polyhybridism.

When the isolate boundaries are completely broken, balance is reached in a single generation as regards monohybrid characters; on the other hand the dilution is not so rapid for polyhybrid characters. To work this out, let us assume that there is an admixture of two populations, in which a dihybrid character occurs in different frequencies. (Cf. *Wahlund*, 1928.)

In diallelic dihybridism we will call the two recessive genes R_1 and R_2, corresponding to the dominant genes D_1 and D_2. The former are assumed to appear in a population with the frequencies r_1 and r_2, the latter with the frequencies d_1 and d_2; $r_1 + d_1 = 1$ and $r_2 + d_2 = 1$. The genes are formed into the gametes R_1R_2, R_1D_2, D_1R_2 and D_1D_2, whose frequencies are denoted $(r_1 r_2)$, $(r_1 d_2)$, $(d_1 r_2)$, and $(d_1 d_2)$ respectively; $(r_1 r_2) + (r_1 d_2) + (d_1 r_2) + (d_1 d_2) = 1$. If the genes should randomly be combined, $(r_1 r_2)$ should be equal to $r_1 r_2$, $(r_1 d_2) = r_1 d_2$, and so on. We will assume, however, that this random situation has been upset by admixture in the population, so that

$$\begin{aligned}(r_1 r_2) &= r_1 r_2 + \Delta_{R_1 R_2},\\ (r_1 d_2) &= r_1 d_2 + \Delta_{R_1 D_2},\\ (d_1 r_2) &= d_1 r_2 + \Delta_{D_1 R_2},\\ (d_1 d_2) &= d_1 d_2 + \Delta_{D_1 D_2}.\end{aligned}$$

By adding these equations in pairs, and using $r_1 + d_1 = 1$, $r_2 + d_2 = 1$, we get:

$$\Delta_{R_1 R_2} = -\Delta_{R_1 D_2} = -\Delta_{D_1 R_2} = \Delta_{D_1 D_2}.$$

The formulæ can thus be written as follows:

$$\begin{aligned}
(r_1 r_2) &= r_1 r_2 + \Delta_{R_1 R_2}, \\
(r_1 d_2) &= r_1 d_2 - \Delta_{R_1 R_2}, \\
(d_1 r_2) &= d_1 r_2 - \Delta_{R_1 R_2}, \\
(d_1 d_2) &= d_1 d_2 + \Delta_{R_1 R_2}.
\end{aligned}$$

We will now assume random crossing in our population. In a given single crossing, a gamete, e.g. $R_1 R_2$, can be passed on *unbroken*. Here we take it that both the genes are got from one of the parents. In such cases the gamete frequency $(r_1 r_2)$ will be unchanged, and $(r_1 r_2) = r_1 r_2 + \Delta_{R_1 R_2}$. As often as not the gamete is *broken*, so that one gene is obtained from each of the parents. Here the genes meet at random with the frequency $r_1 r_2$.

After one crossing, then, the frequency of the gamete $R_1 R_2$, denoted $(r_1 r_2)_1$, is got from the following formula:

$$(r_1 r_2)_1 = r_1 r_2 + \frac{1}{2} \Delta_{R_1 R_2}.$$

After a certain number, n, of crossings (the n^{th} generation), the frequency $(r_1 r_2)_n$ for the gamete $R_1 R_2$ is determined by the formula:

$$(r_1 r_2)_n = r_1 r_2 + \frac{1}{2^n} \Delta_{R_1 R_2}.$$

Now if the formulæ are expanded to apply to all the four sorts of gamete, we get with analogous designations:

$$(r_1 r_2)_n = r_1 r_2 + \frac{1}{2^n} \Delta_{R_1 R_2} = \frac{1}{2^n} (r_1 r_2) + \frac{2^n - 1}{2^n} r_1 r_2, \qquad (73\,a)$$

$$(r_1 d_2)_n = r_1 d_2 - \frac{1}{2^n} \Delta_{R_1 R_2} = \frac{1}{2^n} (r_1 d_2) + \frac{2^n - 1}{2^n} r_1 d_2, \qquad (73\,b)$$

$$(d_1 r_2)_n = d_1 r_2 - \frac{1}{2^n} \Delta_{R_1 R_2} = \frac{1}{2^n} (d_1 r_2) + \frac{2^n - 1}{2^n} d_1 r_2, \quad (73\,c)$$

$$(d_1 d_2)_n = d_1 d_2 + \frac{1}{2^n} \Delta_{R_1 R_2} = \frac{1}{2^n} (d_1 d_2) + \frac{2^n - 1}{2^n} d_1 d_2. \quad (73\,d)$$

The above formulæ show that if alien dihybrid hereditary elements are added to a population, we do not only get the immediate effect they exert direct on its hereditary composition. There is a secondary effect, which is extended over generations. The population is successively changed towards the limit [$(r_1 r_2) \rightarrow r_1 r_2$, $(r_1 d_2) \rightarrow r_1 d_2$ and so on], when the gametes appear in combinations dictated by chance and with frequencies dictated by chance.

This development takes place fairly quickly, at any rate with hereditary conditions of a not very complicated type. (See Table 19.)

In polyhybrid inheritance, then, a population remains heterogeneous for a time, even in panmixia. After an admixture of foreign hereditary elements it develops only gradually towards complete homogeneity—that is to say, towards the state of balance when the genes not only appear at random within the population, but also in random combinations.

How are we now to demonstrate a change of the kind described above? One possibility is to divide up the population into groups with different derivations, and to compare these groups. We separate out those in a population descended from the natives of a certain district, and those descended from immigrants. In the latter group we differentiate smaller groups, where the admixture has taken place in recent generations, and others where it took place further back in time. By investigating the frequency of characters in groups obtained in this way, we can estimate the situation. This way is, of course, extremely irksome. A simpler possibility is to investigate the correlation between different hereditary characters.

TABLE 19.

The proportions of gametes broken to varying degrees in different generations after the population started from.

Number of generations after the original population started from	Dihybrid heredity		Trihybrid heredity			Tetrahybrid heredity				Pentahybrid heredity				
	Unbroken gametes	Totally broken gametes	Unbroken gametes	Once broken gametes	Totally broken gametes	Unbroken gametes	Once broken gametes	Twice broken gametes	Totally broken gametes	Unbroken gametes	Once broken gametes	Twice broken gametes	Thrice broken gametes	Totally broken gametes
1	0.5	0.5	0.25	3 · 0.25	—	0.125	7 · 0.125	—	—	0.0625	15 · 0.0625	—	—	—
2	0.25	0.75	0.0625	3 · 0.1875	0.375	0.0156	7 · 0.0469	6 · 0.0938	0.0938	0.0039	15 · 0.0117	25 · 0.0234	10 · 0.0234	—
3	0.125	0.875	0.0156	3 · 0.1094	0.6563	0.0020	7 · 0.0137	6 · 0.0820	0.4106	0.0003	15 · 0.0017	25 · 0.0103	10 · 0.0513	0.2051
4	0.0625	0.9375	0.0039	3 · 0.0586	0.8203	0.0002	7 · 0.0037	6 · 0.0513	0.6665	0.0000	15 · 0.0002	25 · 0.0032	10 · 0.0417	0.4999
5	0.0313	0.9687	0.0010	3 · 0.0303	0.9082	0.0000	7 · 0.0009	6 · 0.0284	0.8231	0.0000	15 · 0.0000	25 · 0.0009	10 · 0.0257	0.7202
10	0.0010	0.9990	0.0000	3 · 0.0010	0.9971	0.0000	7 · 0.0000	6 · 0.0001	0.9941	0.0000	15 · 0.0000	25 · 0.0000	10 · 0.0010	0.9904

Isolates and race.

Correlation and racial groups.

It has been stated earlier that we can only talk of races provided an isolate or a group of isolates display differences from other isolates. Strictly speaking, we cannot speak of racial characters—only of racial differences. A character which today is regarded as common to the human race, and is consequently not a racial character, may tomorrow become such an one by the discovery of a group of isolates which lack it. One of the reasons why racial differences are of interest is that upon them can be built political and patriotic norms for men's behaviour. Because of this there are reasons for an artificial division of the problem, thus: To what extent do differences occur within a people—i.e. how far is it heterogeneous and built up of isolates, whether social or regional, differing from one another—and to what extent are there differences between two different peoples? Yet in theory both the peoples might be regarded as forming groups of isolates included in a greater population. In practice, however, it is difficult to carry out uniform investigations beyond the boundaries of a given country; consequently most of those carried out with uniform methods come to refer to a single country, and when comparing the populations in two different countries it is at present difficult to reach any conclusions, since there is seldom any good guarantee that the observations were made in a uniform manner.

Now, if there are different races in a population, this must mean that the constitution of groups of isolates differs from one to the other in respect of heredity. This causes a correlation. If we investigate the population in the U.S.A., for example, we will find a correlation between colour of the skin, kinky hair, etc., due to groups of isolates of negroes and whites respectively in the population. If, on the other hand, we find in a population that there is no correlation between physical characters that are regarded of importance from a racial point of view, this means that the population has become homogeneous on account of isolate-breaking; we are then, of course, not justified in speaking of racial differences within the people.

Since isolate-breaking takes place, a diminution of the racial differences between peoples is to be expected. In various countries of Europe there has indubitably been immigration which brought with it the formation of isolates—often social isolates in the form of an upper class of conquerors; the breaking of the isolate has meant that the differences thus arising within the peoples subsequently decreased and disappeared.

If two populations are mixed, a shorter or longer time must elapse before the state of balance to be expected in panmixia is reached. Even in free crossing it takes several generations before a state of balance is reached not only for polyhybrid characters but also for combinations of monohybrid characters.

Let us take a schematic exemple. (Cf. *Wahlund*, 1932.) We will assume a certain "pure race", A, to be the bearer of two monohybrid independent hereditary characters, I and II, determined by the genes A_1 and A_2. Another "pure race", a, does not have these two characters—or, put in another way, is the bearer of the characters non-I and non-II, with the hereditary genes a_1 and a_2. If, now, these two races appear together within one region, race A with the proportion P and race a with the proportion p, $(P+p = 1)$, the following relations will be obtained holding for the total population of the region:

$$\begin{array}{llll} (A_1) = P & (A_1A_2) = P, \\ (a_1) = p & (A_1a_2) = 0, \\ (A_2) = P & (a_1A_2) = 0, \\ (a_2) = p & (a_1a_2) = p. \end{array}$$

(A_1), (A_2), and (A_1A_2) denote respectively the gene frequencies and the frequency of the gene combination which is only found in race A, and which in the population is represented in its frequency P. The frequencies (a_1), (a_2), and (a_1a_2) refer to race a, and thus have the frequency p. The combinations (A_1a_2) and (a_1A_2) are not represented.

Now, if we investigate the correlation between the characters I and II, we get the correlation coefficient R:

$$R = \frac{(A_1A_2) - (A_1) \cdot (A_2)}{\sqrt{(A_1) \cdot (a_1) \cdot (A_2) \cdot (a_2)}} = 1.$$

In the first crossing generation, generation F_1, the following zygotes are obtained:

$(A_1A_1A_2A_2)$ with the frequency P^2,
$(A_1a_1A_2a_2)$ with the frequency $2\,Pp$,
$(a_1a_1a_2a_2)$ with the frequency p^2.

These zygotes give rise to gene combinations whose frequencies are denoted $(A_1A_2)_1$, $(A_1a_2)_1$, $(a_1A_2)_1$, and $(a_1a_2)_1$. It is easy to show that:

$$(A_1A_2)_1 = P^2 + \frac{1}{2}Pp,$$

$$(A_1a_2)_1 = \frac{1}{2}Pp,$$

$$(a_1A_2)_1 = \frac{1}{2}Pp,$$

$$(a_1a_2)_1 = p^2 + \frac{1}{2}Pp.$$

An investigation of the correlation between the characters I and II now gives:

$$R_1 = \frac{(A_1A_2)_1 - (A_1)\cdot(A_2)}{\sqrt{(A_1)\cdot(a_1)\cdot(A_2)\cdot(a_2)}} = \frac{1}{2}.$$

The correlation has dropped from 1 to $\frac{1}{2}$ from the generation we started with to generation F_1.

Let us now change our original assumption as to pure race. We will let A and a denote two populations differing as regards heredity. On account of the heterogeneity in respect of heredity there would then arise in the primary generation a correlation between the characters I and II, where the correlation coefficient, R, is less than 1.

It is not hard to show that, in this case, the correlation coefficient, R_1, drops after one crossing (in generation F_1) to half its original value. Thus we have:

$$R_1 = \frac{1}{2}R.$$

If the mixture of race continues, we get in the n^{th} generation a "residual correlation":

$$R_n = \frac{1}{2^n} R. \tag{74}$$

The mechanism for the correlation changes is analogous with that for the course of development with polyhybrid characters. On this account it is possible, when studying the correlation between hereditary characters, to establish whether the population is to be regarded as homogeneous in respect of heredity, or whether, by virtue of older admixtures, it is heterogeneous and developing towards a state of balance where the genes occur at random and in random combinations.

It is obvious, then, that if no correlation is found between characters in a population, it must be considered as homogeneous in respect of heredity. There is then no reason to speak of different racial elements in it. In a practical investigation it is clear, however, that we cannot use correlations between any characters whatsoever, for example, between length of leg and length of body, since the former is included in the latter. Nor can we use correlations between length of leg and of arm respectively, since here there is probably correlation due to the fact that both these lengths are in part determined by the same genes. On the other hand, there is certainly nothing to stop us using correlation between the colour of the eyes and the length of the body. If we imagine that we mix a short brown-eyed race with a tall, light-eyed one, it is plain that we begin by getting a correlation, so that the brown-eyed persons are at first shorter than the light-eyed ones. When the admixture has reached homogeneity, however, we find no average difference in stature between brown-eyed and light-eyed persons. The correlation between colour of eyes and length of body has disappeared. We might point out that this disappearance comes pretty quickly in free admixture. After only a few generations the correlation is down to such low values that it can hardly be demonstrated statistically, and it is then no longer of practical importance.

It must also be remembered in this connexion that a correlation between properties can also be due to linkage between genes and can, for very rare characters, be dependent on inmarriage.

Finally it may, from a statistical point of view, be stated that if a small number of isolates in a large population differ from one another in constitution, this may not appear when calculating the correlation

unless the large and the small group, when compared, are given the appropriate weight. In other words, the one group may be so large that the correlation that exists cannot be demonstrated in an ordinary calculation.

The correlation of two characters in a population may therefore be due to both characters being caused by a single gene, or by different genes that are linked together. The cause may also be a different gene frequency in the isolates of which the population is composed; this may be occasioned by race differences. If the characters occur rarely, the correlation found may be conditioned by both having a higher frequency among offspring from inmarriage between closely related parents than among individuals whose parents were not related. However, when selecting rare characters we also select material especially from small isolates in which characters caused by mutations will most easily assert themselves. So for this reason, too, a correlation between such characters might be expected. To make this latter point clearer let us suppose that there is a mutation with a frequency of $1 : 10^5$. In a large isolate, a city with a million inhabitants, for instance, there is relatively little prospect that the gene will meet in a double dose. But when a mutation takes place in a small isolate, comprising a few hundred individuals, there are, as we have already emphasized much greater prospects for the mutation gradually to spread and to give rise to character-bearers. A correlation between character-bearers of this type is therefore to be looked for.

Isolates and racial differences.

It has been stated above that, in order to get a more complete view of racial differences, it is necessary to know the genotypes of the different individuals belonging to the two groups of isolates to be compared. We have, furthermore, indicated methods that can be used in an analysis of differences between isolates. But these methods call for information which at present is difficult to obtain. In all circumstances a measure of the size of possible differences between groups of isolates is desirable. On the whole anthropologists have hitherto been content with trying to establish the existence of differences with the help of statistical methods. The fact that an attempt is made in questions of racial differences to decide if a difference has arisen

at random or is statistically significant marks a step forward. A further step should, however, be taken, in an attempt to get an idea of the size of the differences in such a way as to enable comparisons between groups to be made, and so as to be able to evaluate the difference in relation to the joint part of the variation which may exist. The methods given here can, of course, also be used to measure differences of other kinds and may therefore be of more general interest. (Cf. *Dahlberg*, 1941.)

One possibility is to measure racial differences with the help of the frequency with which a certain diagnosis can be made in separate cases. The procedure is then, in principle, as follows. First of all the two populations to be compared are investigated, giving an idea of the frequency of different characters and their variability. The extent to which individuals can with certainty be referred, with the help of separate characters or combination of characters, to the populations to which they belong is then worked out. In other words, individuals are imagined as mixed together in a public square. We then take, for example, their stature. Certain individuals can now be sorted out on the basis of this character. Some are far too short to belong to the one group, or too tall to belong to the other. We then investigate the cephalic index in the same way, and so on. Finally we investigate combinations of characters. It may be impossible to refer a certain individual to any group on his stature or his cephalic index, but it may be that the combination he displays is only found in the one group. As concerns qualitative characters such as the colour of the eyes, we cannot carry out an empirical sorting on these lines if the question is only one of frequency differences between the groups, but we can use these differences to calculate the result we should get on account of them.

If we want to compare two populations (P' and P'') in respect of a character A (A' and A''), measurable quantitatively, we can express the value for each individual in deviations from the mean values of the two combined populations, and give the divergence in units of the standard deviation for the two populations to which the respective individuals belong. We denote the mean value for the combined population:

$$\frac{M'_A + M''_A}{2}.$$

In the population P' the following mean is obtained for the character A' in a series of n' individuals:

$$M' = \frac{1}{n'} \sum^{n'} \frac{A'_i - \frac{M'_A + M''_A}{2}}{\sigma'_A} = \frac{M'_A - M''_A}{2\sigma'_A}.$$

The standard deviation (which is put = 1) will be:

$$\sigma'^2 = E\left[\frac{A'_i - M'_A}{\sigma'_A}\right]^2 = 1.$$

For the population P'' we get the following mean:

$$M'' = \frac{1}{n''} \sum^{n''} \frac{A''_i - \frac{M'_A + M''_A}{2}}{\sigma''_A} = \frac{M''_A - M'_A}{2\sigma''_A}.$$

Here too the standard deviation is put = 1.

If the populations have different mean values, then of course the two new means will have positive and negative signs respectively. If the standard deviations are equal, the means will have the same numerical values.

If we combine N characters, we get the following means for the two populations:

$$M'_s = \sum_{i=1}^{N} \frac{M'_i - M''_i}{2\sigma'_i}, \tag{75a}$$

$$M''_s = \sum_{i=1}^{N} \frac{M''_i - M'_i}{2\sigma''_i}. \tag{75b}$$

As the standard deviations for both the characters = 1, we get in a combination of N characters the standard deviation $\sqrt{N}$, provided there is no correlation between the characters.

If, on the other hand, the characters are correlated, we get a greater standard deviation. If the average correlation between the characters in the populations P' and P'' is r' and r'' respectively, we get the following standard deviations:

$$\sigma'^2 = N + N(N-1)r', \tag{76a}$$

$$\sigma''^2 = N + N(N-1)r''. \tag{76b}$$

In a combination of the characters, it is of course not taken into account that the characters may deviate in opposite directions.

They are added within the groups regardless of signs, and the first character is made to determine which sign it shall be.

The formulæ show that if there are small differences between the populations a sure diagnosis can finally be reached in each separate case by investigating a sufficient number of characters and using combinations of them. This postulates no correlation, however. If the correlation is pronounced, very little is gained by investigating yet another character. If it is slight, the possibilities of diagnosis increase to start with, but after a moderate number of characters have been used the gain is small. If we assume a certain average difference of the means for each new character, we can calculate the smallest number of characters that must be investigated for the two distribution curves to be completely separated, postulating that the range of variation is placed at 6σ. If we call the average difference for each character a, the number of characters N, and the average correlation between these characters r, we can calculate the smallest number required from the following formula:

$$N = \frac{9\,(1 - r)}{a^2 - 9r}. \qquad (77)$$

TABLE 20.

The smallest number of characters required in order to differentiate each individual at different degrees of average correlation (r) and average difference between the means (a). Cf. formula 77.

r = \ a =	0.7	0.8	0.9	1.0	1.1	1.2	1.4	1.6	1.8
0	18.4	14.1	11.1	9.0	7.4	6.3	4.6	3.5	2.8
0.01	22.3	16.2	12.4	9.8	8.0	6.6	4.8	3.6	2.8
0.02	28.5	19.2	14.0	10.8	8.6	7.0	5.0	3.7	2.9
0.03		23.6	16.2	12.0	9.3	7.5	5.2	3.8	2.9
0.04			19.2	13.5	10.2	8.0	5.4	3.9	3.0
0.05			23.8	15.6	11.3	8.6	5.7	4.1	3.1
0.06				18.4	12.6	9.4	6.0	4.2	3.1
0.07				22.6	14.4	10.3	6.3	4.3	3.2
0.08					16.9	11.5	6.7	4.5	3.3
0.09					20.5	13.0	7.1	4.7	3.4
0.10					26.1	15.0	7.6	4.9	3.5
0.12						22.0	9.2	5.4	3.7
0.14							11.1	6.0	3.9
0.16							14.5	6.8	4.2
0.18							21.7	7.9	4.6
0.20								9.5	5.0
0.25								21.8	6.8
0.30									11.7

In Table 20 and Fig. 22 N is calculated according to this formula for different values of a and for the correlation r. a is expressed in units of 2σ. Let us assume that $a = 1$ which means that the differences between the means amount on an average to 2σ and the average correlation $= 0.05$; then we need 16 characters to differentiate each individual in the two populations. If we investigate a smaller number than 16, there will always be a remainder group for which we are unable to make a sure diagnosis. If a amounts to 0.5, i. e. the two means have

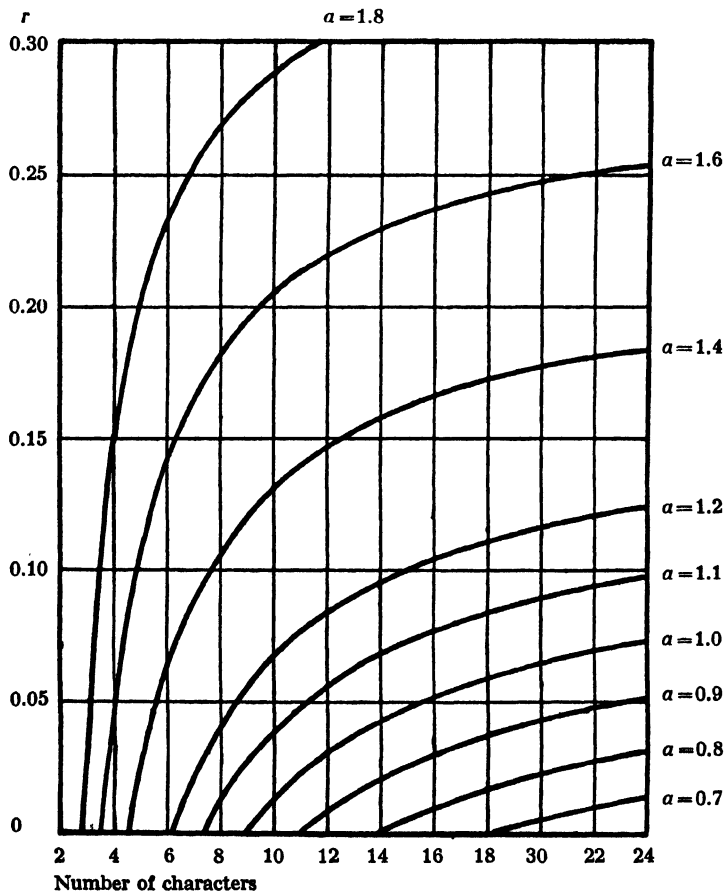


Fig. 22. The smallest number of characters required to differentiate each individual at different degrees of average correlation (r) and average difference between the means (a). Cf. formula 77.

TABLE 21.

The quotient $\frac{\sigma}{N}$ at different degrees of correlation according to the formula $\frac{\sigma}{N} = \sqrt{\frac{N+N(N-1)r}{N^2}}$, when N is the number of characters.

N	$\frac{\sigma}{N}$						
	$r = 0$	$r = 0.05$	$r = 0.10$	$r = 0.15$	$r = 0.20$	$r = 0.25$	$r = 0.30$
2	0.71	0.72	0.74	0.76	0.77	0.79	0.81
3	0.58	0.61	0.63	0.66	0.68	0.71	0.73
4	0.50	0.54	0.57	0.60	0.63	0.66	0.69
5	0.45	0.49	0.53	0.57	0.60	0.63	0.66
6	0.41	0.46	0.50	0.54	0.58	0.61	0.65
7	0.37	0.43	0.48	0.52	0.56	0.60	0.63
8	0.36	0.41	0.46	0.51	0.55	0.59	0.62
9	0.33	0.39	0.45	0.49	0.54	0.58	0.61
10	0.32	0.38	0.44	0.48	0.53	0.57	0.61
11	0.30	0.37	0.43	0.48	0.52	0.56	0.60
12	0.29	0.36	0.42	0.47	0.52	0.56	0.60
13	0.28	0.35	0.41	0.46	0.51	0.55	0.59
14	0.27	0.34	0.41	0.46	0.51	0.55	0.59
15	0.26	0.34	0.40	0.45	0.50	0.55	0.59
∞	0	0.22	0.32	0.39	0.45	0.50	0.55

on an average a difference corresponding to σ, we need 36 characters to get a sure diagnosis of race in each separate case, if there is no correlation.

Table 21 and Fig. 23 also show how much is gained by investigating a further character and using it in combinations. We find that even when the correlation is very slight the gain is very little as we approach about 10 characters.

With the help of the method given, then, we can get an idea of how great the racial difference is. We get a figure of the frequency with which an unquestionable diagnosis of race can be made, and we can here compare empirical and calculated values. The knowledge we possess is completely used by sorting out both according to characters and according to combinations of characters.

Finally an expression of racial differences, can also be reached in another way. We can make the sorting out that gives the best results, i. e. differentiate the individuals according to the boundary that is obtained where the distributions intersect. We then get a figure for the number of cases where we sorted correctly and the number

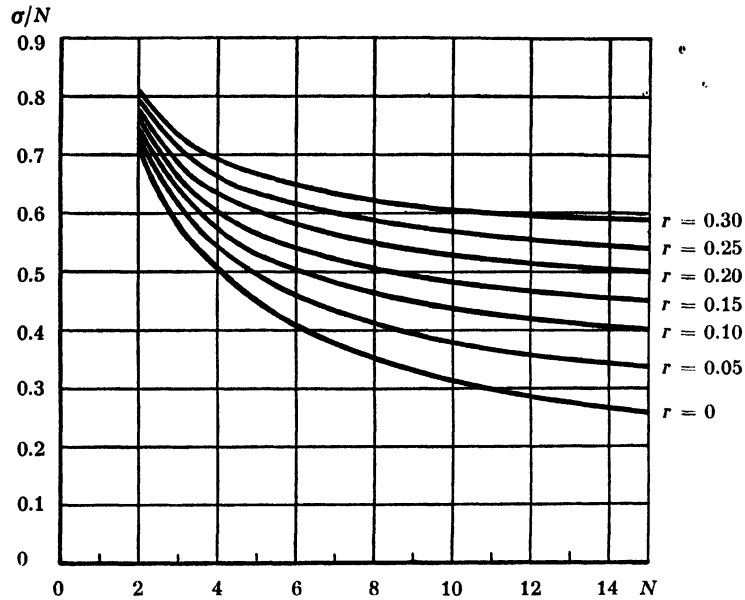


Fig. 23. The quotient $\frac{\sigma}{N}$ at different degrees of correlation and different number of investigated characters.

where we sorted wrong. If the differences are small the sorting will of course turn out more incorrectly than if they are great; if there is no difference, half of the cases will be sorted correctly and half of them wrong. We can, in other words, form a race index $r_i = \frac{p - 50}{50}$ where p is the percent of individuals rightly diagnosed in the best possible division of the material. The method indicated here has been submitted by the author (*Dahlberg*, 1941), and has been used to determine racial differences between Swedes and Laps. The two groups display very great differences, and it is found that by using three characters, stature, cephalic index, and morphological facial index, a sure diagnosis can be made for Laps in 57% of the cases. If we make the best division of the material, we get 93% Laps and 7% Swedes. The racial index is, in other words, 0.86.

As early authors as *Weinberg* (1909) and *Philiptschenko* (1924) have touched on the question of admixture in a population, and shown

that, for polyhybrid characters, a random distribution of the genes is not reached until after several generations. The conception of isolate in human populations has been introduced by *Wahlund* (1928), who gave methods for calculating the deviations from panmixia which the isolate boundaries occasion; he also gave general formulæ for the importance the breaking of isolates has for monohybrid and polyhybrid characters. Formulæ for calculating the size of isolates have been given by *Dahlberg* (1929); the same author (1938) has given special formulæ for calculating the importance of isolate-breaking with very rare monohybrid and polyhybrid characters. Formulæ for the changes of the correlation in isolates have been given by *Wahlund* (1932). *Dahlberg* (1941) has submitted the methods of measuring racial differences described here.

Mutations, selection, and isolates.

When a mutation arises in an isolate, it cannot in the first generation be the subject of selection (unless it is a simple dominant). It can disappear by chance, but it can, also by chance, pass into the next generation. In the latter case it is still free from selection, and this is also the case in the following generation, as marriages between brothers and sisters do not take place among human beings. In the third generation, too, it is practically free, as it is extremely seldom that aunts and uncles marry their nephews and nieces. Only in the fourth generation, following a marriage between cousins, can the mutation be subject to selection. The genes may then unite to form homozygotes.

It should however, be remembered that if the cousins, who are heterozygotes in the fourth generation, are of the same sex, the mutation cannot conceivably be subject to selection after a marriage between cousins. If there are two heterozygotes, the probability of this is $\frac{1}{2}$, and if there are three, $\frac{1}{4}$. All this means that, to start with, mutations are not subject to selection. Only after heterozygosis has reached a certain extent do character-bearers appear who are thus subject.

If the selection is absolute, so that every character-bearer is prevented from propagating, a state of balance will set in at a *minimum heterozygous frequency*, which is determined by the mutation frequency. If we assume a population where the gene is absent to begin with and where a certain mutation frequency appears combined with absolute selection, the heterozygous frequency will slowly rise to the state of balance. If we assume that mutations cease after this has been reached, the heterozygous frequency will slowly decrease and asymptotically approach 0, though this process will, of course, be extremely gradual.

Now, the position of the least heterozygous limit depends not only on the mutation frequency but also on the intensity of the selection, and on the processes present in the population, namely the size of the isolates, assortative mating, and inmarriage. It is, of course, different in different modes of inheritance.

Let us assume that the state of balance lies at a frequency of character-bearers of $1 : N$. If the character is *monohybrid-recessive* and the gene has the frequency r, we get:

$$r^2 = \frac{1}{N}.$$

Therefore, $r = \frac{1}{\sqrt{N}}$. The frequency of heterozygotes, $2rd$, will be:

$$2rd = 2 \cdot \frac{1}{\sqrt{N}} \cdot \left(1 - \frac{1}{\sqrt{N}}\right). \tag{78}$$

If N is a large number, the expression will be approximately:

$$2rd = \frac{2}{\sqrt{N}}.$$

In *polyhybrid recessivity*, when the different genes have the frequencies $r_1, r_2, r_3, \ldots r_n$, the state of balance lies at

$$r_1^2 \cdot r_2^2 \cdot r_3^2 \cdots r_n^2 = \frac{1}{N}.$$

If $r_1 = r_2 = r_3 = \ldots r_n = r$, i.e. every $d_x = d$, we get:

$$r^{2n} = \frac{1}{N} \text{ and } r = \sqrt[2n]{\frac{1}{N}}.$$

The heterozygous frequency will then be:

$$1 - r^{2n} - d^{2n} = 1 - \frac{1}{N} - \left(1 - \frac{1}{\sqrt[2n]{N}}\right)^{2n}. \tag{79}$$

If N is a large number but n is not, we get:

$$1 - r^{2n} - d^{2n} \approx \frac{2n}{\sqrt[2n]{N}}.$$

In *polyhybrid dominance*, when the dominant gene has the frequencies d_1, d_2, d_3, ... d_n, and the recessive gene the frequencies r_1, r_2, r_3, ... r_n, the state of balance will lie at:

$$(d_1^2 + 2r_1 d_1) \cdot (d_2^2 + 2r_2 d_2) \cdots (d_n^2 + 2r_n d_n) = \frac{1}{N}.$$

If $d_1 = d_2 = d_3 = \ldots d_n$, we get:

$$(d^2 + 2rd)^n = \frac{1}{N} \text{ and}$$

$$d = 1 - \sqrt{1 - \frac{1}{\sqrt[n]{N}}} \approx \frac{1}{2\sqrt[n]{N}} \tag{80a}$$

$$\text{and also } r = \sqrt{1 - \frac{1}{\sqrt[n]{N}}} \approx 1 - \frac{1}{2\sqrt[n]{N}}. \tag{80b}$$

The heterozygous proportion at the least heterozygote limit will be:

$$1 - (d^2 + 2rd)^n - r^{2n} = 1 - \frac{1}{N} - \left(1 - \frac{1}{\sqrt[n]{N}}\right)^n \approx \frac{n}{\sqrt[n]{N}}. \tag{81}$$

If we know the frequency of the character-bearers to be subject to selection, we can use these formulæ to calculate the frequency of the genes and of the heterozygotes in the different hereditary mechanisms.

We have previously stated that, at a certain mutation frequency and a certain selection, a state of balance must gradually set in, when the number of individuals eliminated by selection corresponds to the number of mutations in monohybrid dominance and double mutation frequency in monohybrid recessivity. Let us assume that for some reason this state of balance is upset. The gene is assumed to have the frequency r. The mutation frequency is μ. Selection eliminates k of the character-bearers, r^2. In this situation a change from generation to generation takes place. The difference between two consecutive generations is:

$$r_{n+1} - r_n = r_n - kr_n^2 + 2\mu(1 - r_n) - r_n.$$

Seeing that the process approaches the state of balance asymptotically, it will go on infinitely. We can then assume that the time represented by one generation is infinitely small; the difference between two generations can thus be taken as the derivate with respect to time for a function expressing the course of the process. Thus:

$$\frac{dr}{dn} = -kr^2 + 2\mu\,(1-r),$$

$$\therefore dn = -\frac{dr}{k\left(r^2 + \frac{2\mu r}{k} - \frac{2\mu}{k}\right)}.$$

By integration we get:

$$n = -\frac{1}{k}\int_{r_0'}^{r} \frac{dr}{r^2 + \frac{2\mu}{k}r - \frac{2\mu}{k}},$$

$$\therefore n = \frac{1}{2\sqrt{2\mu k + \mu^2}} \log \frac{r - r_2'}{r - r_1'} \cdot \frac{r_0' - r_1'}{r_0' - r_2'}, \tag{82}$$

$$\text{when } r_1' = \frac{\sqrt{2\mu k + \mu^2} - \mu}{k},$$

$$r_2' = -\frac{\sqrt{2\mu k + \mu^2} + \mu}{k},$$

r_0' is the gene frequency found in the primary generation, r_1' is the gene frequency at the state of balance, and r is a value between these, for which we will compute the time. It must be remembered that the equation cannot be used when r_0' approaches r_1'. We have assumed that the time one generation represents is very small in relation to the time elapsing before the state of balance is reached; this is not the case for extremely small differences from the state of balance. We have then no right to consider the discontinuous function to be continuous. For the rest, the equation shows that if r_0' deviates from r_1', but $r_1' = r$, i.e. the value we are looking for is the frequency at balance between selection and the mutation, n will be ∞. This means that the state

of balance is only reached at infinity. It is therefore of interest to calculate the time which elapses before the state of balance is half reached, i.e. till that frequency which is the mean of the primary value and the frequency at balance. Assume that $r'_0 = cr'_1$ and thus:

$$r = \tfrac{1}{2} r'_1 (c+1).$$

We then get

$$n = \frac{1}{2\sqrt{2\mu k + \mu^2}} \log \frac{\frac{1}{2} r'_1 (c+1) - r'_2}{\frac{1}{2} r'_1 (c+1) - r'_1} \cdot \frac{cr'_1 - r'_1}{cr'_1 - r'_2} =$$

$$= \frac{1}{2\sqrt{2\mu k + \mu^2}} \log \frac{r'_1 (c+1) - 2r'_2}{cr'_1 - r'_2}. \tag{83}$$

If $k = 1$, i.e. if there is total selection, and if $\sqrt{2\mu} \ll 1$ we get:

$$r'_1 \approx \sqrt{2\mu} \text{ and } r'_2 \approx -\sqrt{2\mu},$$

$$\therefore n = \frac{1}{2\sqrt{2\mu}} \log \frac{3+c}{1+c}. \tag{84a}$$

If $k = 1$ and $\sqrt{\frac{2\mu}{k}} \ll 1$ we get:

$$r'_1 = \sqrt{\frac{2\mu}{k}} \text{ and } r'_2 = -\sqrt{\frac{2\mu}{k}},$$

$$\therefore n = \frac{1}{2k\sqrt{\frac{2\mu}{k}}} \log \frac{3+c}{1+c}. \tag{84b}$$

We can with the help of these expressions calculate the number of generations needed for a change from a certain frequency of character-bearers to another frequency. We have previously asserted that the frequency of very rare monohybrid characters in a number of Western European countries may possibly have decreased to half that of about

50 years ago, on account of isolate-breaking. It will take infinite time before the state of balance is again achieved. It may, however, be of interest to calculate the time it takes to halve the distance between the present frequency and the frequency of the state of balance. If the original frequency is $r^2 = 2\mu$ and the present frequency is $\frac{r^2}{2}$, halfway between them is:

$$r\left(\frac{1}{2\sqrt{2}} + \frac{1}{2}\right) = \sqrt{\mu}\left(\frac{1}{2} + \frac{1}{\sqrt{2}}\right).$$

We require, further, a value for the mutation frequency. *Haldane* has made approximate, and naturally extremely uncertain calculations, giving as a result a mutation frequency of $1 : 10^5$. If we assume total selection, we find with the help of formula 84a that, after 123 generations, the difference has been levelled out by half: this if we reckon 25 years to a generation, would correspond to 3000 years. The calculation gives a notion of how slowly the mutation frequency levels out a deviation from the state of balance.

Haldane (1939 and 1940) has carried out a similar calculation, starting from the view that there is in a population a certain amount of inmarriage greater than would be expected in panmixia, and that the state of balance prevailing in this situation is changed by a change of the inmarriage frequency. The calculations he made give figures of the same order of magnitude.

We have above discussed mutation frequency and selection assuming that the processes take place in very large populations and for long periods of time. Actually, of course, the populations are limited; not only this, they are divided up into isolates of moderate size. The frequency that genes arising through mutation have in the isolates will, as a matter of fact, be very much conditioned by chance. If a heterozygote results from mutation, the probability that the gene will disappear and not be represented in the next generation is one quarter if each marriage has, on an average, two children who reach sexual maturity. In addition to this, the heterozygote in question may for some reason be sterile, or not contract a marriage. In actual fact, the gene runs a risk of disappearing by chance at the transition to each new generation, but it may also happen to increase in frequency. In small populations there is also the possibility that the gene increases

in frequency to such an extent as to give homozygosis; this means that its allelomorph disappears at random. Processes of this kind can probably play an important part for animals and plants. The first to point out this possibility was *Hagedoorn* (1921). Subsequently *Sewall Wright* (1921, 1930, 1931, 1932, 1934, 1935) and *R. A. Fisher* (1928, 1930, 1931) analysed the problem mathematically from several aspects. *Dobzhansky* (1937) has discussed the problem against the background of empirical investigations, and reviewed the literature in this field.

As regards man, there is hardly reason to reckon with random increase of mutations, giving rise to homozygosis, within isolates in civilized populations. On the other hand, there is no doubt that the opposite possibility—a random disappearance of mutations—is of importance; we must therefore take into account that certain genes are completely lacking in certain isolates, and have a larger or smaller frequency in others—that is to say, that that situation arises which the author earlier on assumed to obtain for genes of certain rare defects. But it can hardly be of interest to review in this connexion the mathematical expositions that have been made. Those who are interested are referred to the literature quoted, above all to the work of *Dobzhansky*.

Isolates and inmarriage.

When the effect of inmarriage was calculated no account was taken of the fact that the population is divided up into isolates. The isolate boundaries imply, however, that there is a certain limit to the rarity of a gene. For a gene to be able to exist in an isolate at all, there must be at least one heterozygote per generation, and before a character-bearer can appear in an isolate there must be at least two. Further, we have to take into account that the frequency of inmarriage depends on the size of the isolate. In small isolates it occurs to a relatively great extent. In large isolates it is low, since the possibility of marrying others than relatives is larger.

To get an idea of the part inmarriage plays in populations formed from isolates we can take formulæ used earlier. According to formula 45 the proportion of the character-bearers, k, deriving from parents who are cousins, is:

$$k = \frac{c\,(1 + 15\,r)}{16\,r}.$$

In panmixia, the frequency of cousin marriages, c, if the average number of children is b (formula 60) is:

$$c = \frac{2\,b\,(b-1)}{n-1}.$$

For a character-bearer to arise, there must be at least two heterozygotes in an isolate. In this situation, the gene frequency, r, if the number of individuals in the isolate is n, is:

$$r = \frac{1}{n}.$$

If these values are inserted in the formula, we get:

$$k = \frac{b\,(b-1)\,(n+15)}{8\,(n-1)}. \qquad (85)$$

If b is 2, which implies that the population is constant, the formula will be as follows:

$$k = \frac{n+15}{4\,(n-1)} = \frac{1}{4}\left(1 + \frac{16}{n-1}\right)$$

and when $n-1 \approx n$, then

$$k \approx \frac{1}{4}\left(1 + \frac{16}{n}\right).$$

If we assume on an average 4 heterozygotes in each isolate where character-bearers arise, we get:

$$r = \frac{2}{n}.$$

If this value is inserted in the formula, it will become:

$$k = \frac{n+30}{8\,(n-1)} \text{ and } k \approx \frac{1}{8}\left(1 + \frac{31}{n}\right). \tag{86}$$

On the basis of the two formulæ given, the values for the percent deriving from marriages between cousins at different sizes of the isolate are shown in Table 22 and Fig. 24. The boundary value, which is

TABLE 22.

Percentage of character-bearers deriving from marriages between cousins when such marriages have a random frequency and the isolates are of varying size (n). We assume that the number of children is 2 and that in each isolate there are 2, respectively 4, heterozygotes. Cf. formula 85.

Size of the isolates = n	2 heterozygotes per isolate	4 heterozygotes per isolate
10	0.6945	0.5556
25	0.4167	0.2865
50	0.3316	0.2041
100	0.2875	0.1625
250	0.2650	0.1400
500	0.2575	0.1325
1 000	0.2538	0.1288
5 000	0.2508	0.1258
10 000	0.2504	0.1254
∞	0.2500	0.1250

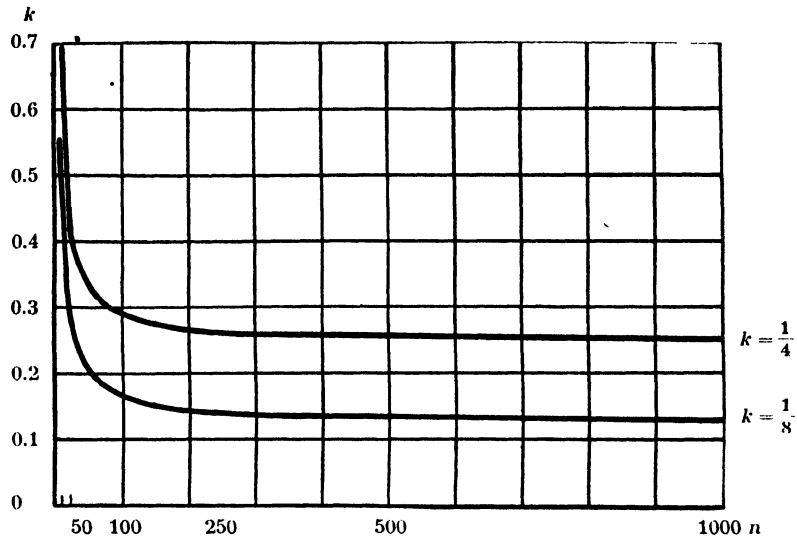


Fig. 24. Percentage of character-bearers deriving from marriages between cousins when such marriages have random frequency and the isolate is of varying size (n). We assume that the number of children is 2 and that there are 2, respectively 4, heterozygotes in each isolate. Cf. formula 95.

obtained if $n = \infty$, is in the one case 25 %, and in the other 12.5 %. The value remains constant, practically speaking, if the size of the isolate decreases. Only in very small isolates of less than 100 individuals does any noticeable difference arise. When $n = 25$, 42 % are descended from marriages between cousins in the first case, and 29 % in the second.

We should therefore have most reason to expect values between 15% and 30%. This agrees with the figures obtained when investigating a number of rare characters. By way of example it may be mentioned that in juvenile amaurotic idiocy 15% of the character-bearers are descended from cousins, in retinitis pigmentosa 17 %, albinism 17 %, Friedreich's ataxia 9 %, etc. The empirical figures seem, in other words, to be somewhat lower than the first formula would lead one to expect; this indicates that there are on an average (if marriage between cousins has a random frequency) rather more than 2 heterozygotes in the isolates.

The formulæ and the empirical figures available indicate primarily that a prohibiting of marriages between cousins would diminish the frequency of character-bearers by 15 %. For the rest the formulæ imply that the frequency of marriages between cousins and the gene frequency

balance one another. If a gene is very rare and the frequency of cousin marriages very high, a large proportion of the character-bearers would come from such marriages; in theory, then, the prohibition of marriages between cousins would, in such a situation, have a far greater effect than the one given. We cannot, however, expect to get both a high frequency of cousin marriages and a very low gene frequency. If an isolate is small we get a high frequency of such marriages, but a gene cannot then be very rare, since the isolate must contain at least 2 heterozygotes. If an isolate is large, the gene may be very rare, but we cannot in that case expect to have a high frequency of marriages between cousins.

We have stated earlier on, however, that in certain populations the marriages between cousins may nevertheless have a higher frequency than the one to be expected in panmixia. This should in particular hold in populations where the parents decide the marriages of their children. Even if the isolates are large, we can expect a relatively high frequency of cousin marriages, though it is probably influenced to a certain extent in such populations by isolate-breaking. This doubtless makes for a diminished contact between members of the same family, which has an indirect effect. If the marriages between cousins are more frequent than would be expected in panmixia, we naturally get a greater effect by prohibiting them than was given above. At present, however, there are no empirical data on which to base a calculation of the effect in a population of this kind, so that we really have no call to go into this side of the matter in more detail.

We have used the marriages between cousins to get an idea of the breaking of isolates. When assessing this process it is to a certain extent a matter of taste whether we in the first place take inmarriage and investigate what importance its decrease has for the frequency of characters. Since it is only possible to get data as to inmarriage of the closer degree (marriages between cousins), we have to ignore all more distant degrees. We have stated earlier on that, in principle, all marriages are consanguineous, since if it is assumed that no kinship ever existed between the individuals in earlier generations, a calculation of their numbers would very soon bring us to astronomical figures, whereas in point of fact these numbers were undoubtedly smaller than those of the generation now living.

If, on the other hand, we assume that isolate boundaries have existed and been broken, and that there was inmarriage to the extent of a

random amount in respect of the boundaries existing, we subscribe to what has actually happened. However, we schematize the situation by assuming isolates with sharp boundaries in the same way as we schematize the situation when we speak of sharply demarcated generations; in point of fact the generations merge into one another imperceptibly. In most cases, however, a schematization of this kind would not give misleading results.

A special case of theoretical interest is constituted by a sharply demarcated isolate (e.g. the population of an island) which increases in size on account of a high birth-rate. In an isolate like this we would expect to find the frequency of cousin marriages diminishing, while the frequency of more distant consanguineous marriages increases. The balance is maintained by no change in the frequency of genes and character-bearers respectively. If the population is regarded as an isolate, we have the immediate result that the frequency of character-bearers is constant, while on the other hand an investigation of the frequency of cousin marriages would easily mislead us into concluding that the frequency of the character-bearers has diminished because we cannot pay regard to more distant degrees of inmarriage. As *Haldane* affirmed, both views may have special advantages in different situations. It may therefore be advisable to apply both when solving the problem; in all circumstances it must be remembered that in both cases special assumptions are made, and a schematic view of the matter applied.

It is of practical interest to try and reach some idea of the importance that conscious measures against inmarriage may be thought to have. Measures against distant degrees are then hardly conceivable. Close consanguineous marriages, as between brothers and sisters and the like, are practically non-existent in human populations. In practice, all that remains is to forbid marriage between cousins. At the present time there are different laws in different countries; in some such marriages are forbidden, even though dispensations may by granted to a certain extent; in others, again, they are permitted. The Roman Catholic Church is against marriage between cousins in principle, but grants dispensation. Our concern is, then, to try and find what the prohibiting of cousin marriages may be thought to imply. It is at once plain from what has already been said that measures have no noteworthy effect on ordinary characters, but have some effect on less ordinary ones. We have shown above that this effect can be expected to be 15–30 % for very rare

characters. It has been stated earlier that inmarriage does not greatly affect one single character. If the character is common, the effect is negligible. If the character is rare, the effect is greater, but then the character is of no importance for the composition of the population. A prohibiting of marriages between cousins does not affect only one character, however; it also exerts an influence on all rare characters. This means that the sum of rare hereditary defects decreases by at most 15–30 %. We may remember in this connexion that, in dealing with a number of groups of defects, which in official statistics are registered under one title, e.g. blind, crippled, imbecile, etc., we have to take into account that the group actually consists of defective individuals of different kinds. Those with hereditary blindness, who naturally only constitute a part of all the blind, are made up of different kinds of defects, each one of which is very rare. The same is probably true of imbeciles and cripples in the extent to which hereditary characters are in question. The situation of deaf-mutes has scarcely been worked out yet, but it is possible that this group is more uniform. By forbidding marriages between cousins, it should thus be possible to attain a noticeable effect on the sum of the defective. This effect is reached after one generation, after which nothing is gained by continuing the measures. If inmarriage is again allowed, the high frequency will return. The conceivable gain must, however, be weighed up against the possible loss due to the fact that rare characters of a favourable kind also diminish in frequency. As far as special talent is conditioned by rare monohybrid recessive genes, it, too, can be expected to diminish. However, it is not likely that special talent is inherited in this simple way. (It is, of course, also conceivable that certain defects have a more complicated hereditary mechanism, though most of them seem to have a simple one.) The effect is less for characters of polyhybrid nature than for monohybrid characters. Our knowledge of the way in which characters are inherited is at present deficient, and special investigations are no doubt required before a definite opinion is reached on them. We have in this connexion only wished to indicate certain relevant points of view. For the sake of completeness it may also be pointed out that social viewpoints must, of course, also be taken into account. No direct estimate can be made of what it means to individuals to have their freedom of action restricted by the prohibition of marriages between cousins, but this side of the matter is, naturally, not to be ignored.

Isolates, assortative mating, and selection.

Earlier on we have analysed assortative mating under panmixia. Even if the population falls apart into isolates, it is still justifiable in certain situations, e.g. concerning assortative mating between tall and short persons, to disregard the isolate boundaries.

In certain cases, however, isolate influences—which are of considerable importance—must be taken into account. We can differentiate between two mechanisms of somewhat different type. To exemplify the one we can take conditions obtaining for deaf-mutes. These come together to a great extent through their special organizations. They are sufficiently numerous to meet to a relatively large extent, at any rate in densely populated places. Some of them owe their affliction to environmental factors, others to hereditary factors. In such conditions the situation is that the deaf-mutes form an isolate recruited from a greater or lesser part of the hereditary deaf-mutes (a number of them are at large in the population and more or less isolated from their fellow sufferers). The isolate also contains persons who are not hereditarily deaf and dumb (deaf-mutes due to environment), and whose genetical constitution is the same as that of the normal population. In this case the isolate is formed anew in each generation. Here it is, of course, a matter of taste whether we speak of assortative mating and isolate influence, or selective isolate influence.

An example of the other mechanism is the formation of a social class. In so far as special characters are required for a person to be able to work his way up from a lower class of society to a higher one and cross more or less sharp isolate boundaries, there are selective isolates of different composition in respect of heredity. Here, too, we can talk of assortative mating which goes on with the help of isolate boundaries. In contradistinction to defect isolates, these isolates are not formed afresh for each generation but have a more permanent character.

Assortative mating through defect isolates.

We will assume that assortative mating in defect isolates brings the frequency of character-bearers for a monohybrid recessive character

TABLE 23.

Cf. the text.

Composition of marriage	Frequency in the defect isolate	Children		
		Frequency of the types		
		RR_n	RD_n	DD_n
$RR_{n-1} \times RR_{n-1}$	$k_1^2 (r^2 + \Delta)^2 = a$	a		
$RR_{n-1} \times RD_{n-1}$	$2 k_1 k_2 (r^2 + \Delta)(2rd - 2\Delta) = b$	$\frac{1}{2}b$	$\frac{1}{2}b$	
$RR_{n-1} \times DD_{n-1}$	$2 k_1 k_2 (r^2 + \Delta)(d^2 + \Delta) = c$		c	
$RD_{n-1} \times RD_{n-1}$	$k_2^2 (2rd - 2\Delta)^2 = d'$	$\frac{1}{4}d'$	$\frac{1}{2}d'$	$\frac{1}{4}d'$
$RD_{n-1} \times DD_{n-1}$	$2 k_1 k_2 (2rd - 2\Delta)(d^2 + \Delta) = e$		$\frac{1}{2}e$	$\frac{1}{2}e$
$DD_{n-1} \times DD_{n-1}$	$k_2^2 (d^2 + \Delta)^2 = f$			f
	Total	$RR_n = a + \frac{1}{2}b + \frac{1}{4}d'$	$RD_n = \frac{1}{2}b + c + \frac{1}{2}d' + \frac{1}{2}e$	$DD_n = \frac{1}{4}d' + \frac{1}{2}e + f$

TABLE 24.

Cf. the text.

Composition of marriage	Frequency in the remaining population	Children		
		Frequency of the types		
		RR_n	RD_n	DD_n
$RR_{n-1} \times RR_{n-1}$	$(1-k_1)^2 (r^2+\Delta)^2 = a$	a		
$RR_{n-1} \times RD_{n-1}$	$2(1-k_1)(1-k_2)(r^2+\Delta)(2rd-2\Delta) = b$	$\frac{1}{2}b$	$\frac{1}{2}b$	
$RR_{n-1} \times DD_{n-1}$	$2(1-k_1)(1-k_2)(r^2+\Delta)(d^2+\Delta) = c$		c	
$RD_{n-1} \times RD_{n-1}$	$(1-k_2)^2 (2rd-2\Delta)^2 = d'$	$\frac{1}{4}d'$	$\frac{1}{2}d'$	$\frac{1}{4}d'$
$RD_{n-1} \times DD_{n-1}$	$2(1-k_2)^2 (2rd-2\Delta)(d^2+\Delta) = e$		$\frac{1}{2}e$	$\frac{1}{2}e$
$DD_{n-1} \times DD_{n-1}$	$(1-k_2)^2 (d^2+\Delta)^2 = f$			f
	Total	RR_n $a+\frac{1}{2}b+\frac{1}{4}d'$	RD_n $\frac{1}{2}b+c+\frac{1}{2}d'+\frac{1}{2}e$	DD_n $\frac{1}{4}d'+\frac{1}{2}e+f$

after n generations to $r^2 + \Delta_n$. The frequency for the heterozygotes is then $2rd - 2\Delta_n$, and for the dominant homozygotes $d^2 + \Delta_n$. We will assume further that a proportion, k_1, of the recessive character-bearers is included in the defect isolate, and that k_2 of the heterozygotes and the dominant homozygotes are included also. We then get in the isolate the composition of the marriages given in Table 23, in which the constitution of the offspring is also given.

The offspring will display the defect in the following frequency:

$$r^2_{a\,(n+1)} = \frac{[k_2 r + (k_1 - k_2)\ r_n^2]^2}{k_2 + (k_1 - k_2)\ r_n^2}. \tag{87}$$

The character of the marriages and the offspring in the remaining population is given in Table 24.

The offspring will thus display the recessive character in the following frequency:

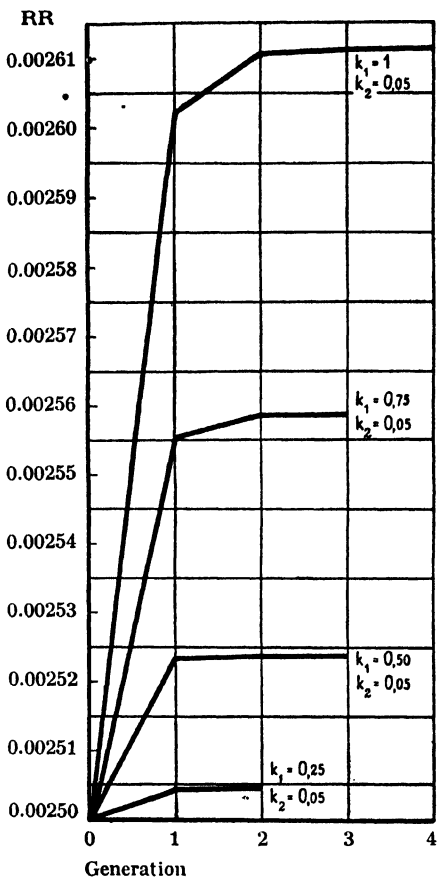
$$r^2_{b\,(n+1)} = \frac{[(1 - k_2)\ r - (k_1 - k_2)\ r_n^2]^2}{(1 - k_2) - (k_1 - k_2)\ r_n^2}. \tag{88}$$

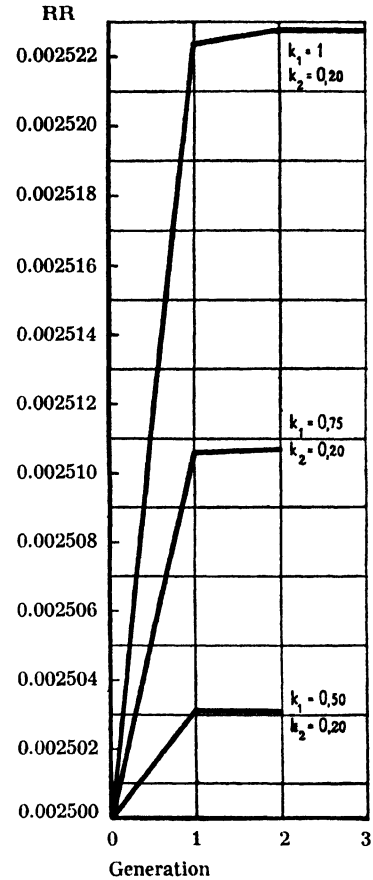
TABLE 25.

Frequency of character-bearers in total populations when assortative mating occurs in defect isolates with varying values of k_1 and k_2 after a different number of generations: RR_0, RR_1, RR_2, RR_3 and RR_4. The calculations have been carried on practically to the state of balance. Cf. formula 89.

k_1	k_2	RR_0	RR_1	RR_2	RR_3	RR_4
0.25	0.005	0.0025	0.00256066	0.00256348	0.00256363	0.00256363
	0.05	0.0025	0.00250471	0.00250472	0.00250472	—
	0.20	0.0025	0.00250009	0.00250009	—	—
0.50	0.005	0.0025	0.00268387	0.00270913	0.00271275	0.00271321[1]
	0.05	0.0025	0.00252355	0.00252399	0.00252400	0.00252400
	0.20	0.0025	0.00250316	0.00250317	0.00250317	—
0.75	0.005	0.0025	0.00295935	0.00311267	0.00316800	0.00318810[2]
	0.05	0.0025	0.00255633	0.00255885	0.00255894	0.00255897
	0.20	0.0025	0.00251061	0.00251070	0.00251070	
1.00	0.005	0.0025	0.00325140	0.00365683	0.00389513	0.00404093[3]
	0.05	0.0025	0.00260257	0.00261096	0.00261166	0.00261172
	0.20	0.0025	0.00252240	0.00252280	0.00252280	—

[1] State of balance arrived at after generation RR_5 : 0.0027133.
[2] » » » » » » » RR_9 : 0.0031996.
[3] » » » » » » » RR_{13}: 0.0042917.





Figs. 25 and 26. Frequency of character-bearers in total populations when assortative mating occurs in defect isolates with varying values of k_1 and k_2 after a different number of generations: RR_0, RR_1, RR_2, RR_3 and RR_4. The calculation has been carried on practically to the state of balance.

Thus we get the following recursion formula for the entire population:

$$r_{n+1}^2 = \frac{[k_2 r + (k_1 - k_2) r_n^2]^2}{k_2 + (k_1 - k_2) r_n^2} + \frac{[(1 - k_2) r - (k_1 - k_2) r_n^2]^2}{(1 - k_2) - (k_1 - k_2) r_n^2}. \quad (89)$$

The values in Table 25 and Figs. 25 and 26 have been calculated with the help of these formulæ. It is seen that a state of balance is reached after a comparatively small number of generations.

We have not taken into account the fact that we can expect the character-bearers, whether determined by heredity or not, to have a lower fertility than individuals lacking the character. For example, deaf-mutes marrying one another can be expected to have a relatively low fertility, partly for economic reasons, partly, too, for reasons of eugenics. Nowadays a number of them know that their affliction may be inherited and consequently involves the risk of burdening their children; they may therefore deliberately restrict their fertility. If the defective individuals have a particularly low fertility, this of course implies a selection, which diminishes the frequency of the hereditarily determined character-bearers who have the defect, and also that of the heterozygotes. A selection working in association with assortative mating through the new formation of isolates has, in principle, the same effect as selection in panmixia. When the character-bearers begin to be rare, they will practically all have come from parents who are heterozygotes. We reach equilibrium between selection and mutation frequency, and the frequency of heterozygotes at this state of balance will be lower than at the same state of balance in panmixia. Assortative mating brings the selection somewhat more quickly up to this state of balance, but for rare characters the difference is not important.

A process of the kind discussed here may to a certain extent be expected to play a part not only for characters with the nature of defects, but also for such as are linked up with special trends of interest, in so far as these are determined by heredity. For example, we can expect musical persons to meet to a particular extent in certain circles and organizations, on account of their interests. It must probably also be taken into account, however, that even in communities where there are more or less pronounced musical isolates, assortative mating between musical people at the same time takes place to a certain extent outside these isolates also. At the present, however, there are no data for estimating the importance of "interest isolates" in assortative mating; nor has it been worked out in more detail how far special interests are determined by heredity.

Assortative mating and social isolates.

The idea is widespread that there is a difference in the hereditary constitution of different classes of society. The upper classes are thought to form a selection of certain advantageous characters. As regards these

ideas it is of interest to try and work out what effect is had by assortative mating beyond isolate boundaries, or by selection in the formation of isolates. Here, too, it is a question of taste whether we put the main stress on selection, or whether we wish to regard the process as a special kind of assortative mating.

We will start with the assumption that there was originally panmixia, and that the population was divided up into two classes; one of these can be assumed to be comparatively small, but both had originally the same gene constitution. We will further assume a certain circulation between the two isolates, so that persons with a given monohybrid character from the larger isolate have a certain possibility of coming to belong to the smaller one. This means we disregard the possibility of persons being brought over at random to the smaller isolate and of persons without the character in question being taken over at random to the larger one. We assume, in other words, that these two changes balance one another. Should this not be so, however, it does not fundamentally affect the nature of the process we are trying to investigate. The transference of certain character-bearers which we have assumed means that the smaller isolate grows at the expense of the larger.

The one isolate, then, is exclusively subjected to a negative selection and is deprived of character-bearers of a certain type. (This isolate thus corresponds to the lower class, which is deprived of talents which work their way up.) We can then use the earlier formulæ for selection (formula 29). If the recessive character has the frequency r, and a proportion, k, of the character-bearers are removed from an isolate, the following formula holds in monohybrid recessivity and in dominance:

$$r_{n+1}^2 = \frac{r_n^2(1-kr_n)^2}{(1-kr_n^2)^2}.$$

If the selection concerns the dominant character, the frequency of genes and characters respectively will progressively decrease. Provided the character in question is rare, we can reckon in practice on the character practically always appearing in a heterozygote form, and the change will run fairly proportional to the strength of the selection present. If, for example, $\frac{1}{10}$ of the character-bearers are transferred per generation to the smaller isolate, in about 10 generations the character will have been practically eradicated in the large isolate. This case is

TABLE 26.

Cf. the text.

Composition of marriage	Frequency in the small isolate	Children		
		Frequency of the types		
		RR_n	RD_n	DD_n
$RR_{n-1} \times RR_{n-1}$	$(A_n x_n^2 + B_n k r_n^2)^2 = a$	a		
$RR_{n-1} \times RD_{n-1}$	$2(A_n x_n^2 + B_n k r_n^2)\, 2 A_n x_n y_n = b$	$\frac{1}{2} b$	$\frac{1}{2} b$	
$RR_{n-1} \times DD_{n-1}$	$2(A_n x_n^2 + B_n k r_n^2)\, A_n y_n^2 = c$		c	
$RD_{n-1} \times RD_{n-1}$	$4 A_n^2 x_n^2 y_n^2 = d'$	$\frac{1}{4} d'$	$\frac{1}{2} d'$	$\frac{1}{4} d'$
$RD_{n-1} \times DD_{n-1}$	$4 A_n^2 x_n y_n^2 = e$		$\frac{1}{2} e$	$\frac{1}{2} e$
$DD_{n-1} \times DD_{n-1}$	$A_n^2 y_n^2 = f$			f
Total		RR_n $a + \frac{1}{2} b + \frac{1}{4} d'$	RD_n $\frac{1}{2} b + c + \frac{1}{2} d' + \frac{1}{2} e$	DD_n $\frac{1}{4} d' + \frac{1}{2} e + f$

of small interest, however, since the characters in question can hardly be thought to be inherited in this way. More reasonably we should consider characters which are inherited in a more complicated fashion. It is therefore more interesting to investigate the effect of selection for a recessive character. The same conditions obtain for characters which are inherited in a complicated way, e.g. dihybrid dominant characters, as for monohybrid recessive characters.

We will assume a small isolate, A, to which recessive character-bearers are added from another isolate B, where $B + A = 1$. We will assume further that the recessive gene in B has the frequency r, and that A has the recessive gene with the frequency x and the dominant gene with the frequency y. Thus $x + y = 1$. We assume as before that k of the character-bearers in B are transferred to A. The composition of the marriages and offspring in the smaller isolate is shown by Table 26.

From this we get the following recursion formula:

$$x_{n+1}^2 = \left[\frac{A_n x_n + B_n k r_n^2}{A_n + B_n k r_n^2}\right]^2 \tag{90}$$

where r_n is obtained from formula 29, given above, and

$$A_{n+1} = A_n + B_n k r_n^2$$

and also

$$B_{n+1} = B_n (1 - k r_n^2).$$

The total frequency of character-bearers in the whole population, p_n, will be:

$$p_n = B_n r_n^2 + A_n x_n^2. \tag{91}$$

The formulæ above have been used to calculate the values in Tables 27, 28, and 29. We have contented ourselves with taking one character which is so rare that in panmixia it would appear in 1 in 1000 of the population; we have further assumed that the small isolate forms 5% of the population, so that the large one forms 95%. Cf. Figs. 27 and 28.

If we look at the lower class first, we find that a slight selection has a very small effect. If 1% of the character-bearers go over to the upper class isolate per generation, their frequency in the lower class will

TABLE 27.

Composition of the lower class in successive generations when it embraces 95 % of the population, the character-bearers at the start have the frequency 1 ‰, and the transference to the upper class has the frequency 1 % ($k = 0.01$) to 100 % ($k = 1$), according to formula 29. The figures in the table are also valid for partial selection of varying strength in regard to a recessive, monohybrid character in the population.

Gen.	$k = 0.01$	$k = 0.05$	$k = 0.10$	$k = 0.25$	$k = 0.50$	$k = 1$
0	0.0010000	0.0010000	0.0010000	0.0010000	0.0010000	0.0010000
1	0.0009994	0.0009969	0.0009939	0.0009847	0.0009696	0.0009396
2	0.0009988	0.0009939	0.0009878	0.0009698	0.0009406	0.0008846
3	0.0009982	0.0009909	0.0009818	0.0009552	0.0009129	0.0008329
4	0.0009976	0.0009879	0.0009759	0.0009410	0.0008864	0.0007868
5	0.0009970	0.0009849	0.0009700	0.0009271	0.0008612	0.0007445
6	0.0009964	0.0009819	0.0009642	0.0009135	0.0008368	0.0007055
7	0.0009958	0.0009789	0.0009584	0.0009002	0.0008134	0.0006695
8	0.0009952	0.0009759	0.0009527	0.0008871	0.0007910	0.0006362
9	0.0009946	0.0009730	0.0009470	0.0008743	0.0007695	0.0006053
10	0.0009940	0.0009701	0.0009414	0.0008618	0.0007489	0.0005766
15	0.0009910	0.0009556	0.0009140	0.0008031	0.0006572	0.0004596
20	0.0009880	0.0009415	0.0008878	0.0007503	0.0005812	0.0003749

TABLE 28.

Composition of the upper class in successive generations when it embraces 5 % of the population, the character-bearers at the start have the frequency 1 ‰, and, further, the transference to the upper class has the frequency 1 % ($k = 0.01$) to 100 % ($k = 1$), according to formula 90.

Gen. x^2	$k = 0.01$	$k = 0.05$	$k = 0.10$	$k = 0.25$	$k = 0.50$	$k = 1$
0	0.001000	0.001000	0.001000	0.001000	0.00100	0.00100
1	0.001011	0.001059	0.001119	0.001309	0.00165	0.00243
2	0.001023	0.001119	0.001244	0.001649	0.00242	0.00428
3	0.001035	0.001181	0.001373	0.002020	0.00330	0.00640
4	0.001046	0.001244	0.001508	0.002419	0.00425	0.00872
5	0.001058	0.001308	0.001649	0.002842	0.00528	0.01117
6	0.001070	0.001374	0.001793	0.003288	0.00637	0.01368
7	0.001081	0.001441	0.001943	0.003755	0.00751	0.01624
8	0.001093	0.001509	0.002097	0.004242	0.00868	0.01881
9	0.001105	0.001579	0.002255	0.004746	0.00989	0.02136
10	0.001117	0.001649	0.002417	0.005267	0.01112	0.02389
15	0.001178	0.002019	0.003284	0.008064	0.01747	0.03582
20	0.001241	0.002417	0.004238	0.011088	0.02384	0.04630

TABLE 29.

Composition of the total population, when it is divided up into an upper class which embraces 5 % of the population and a lower class embracing 95 % of the population and when the character-bearers at the start have the frequency 1 ‰ in different strength of a selective transference from the lower class to the upper class ($k = 0.01$ to $k = 1$). Cf. formula 91.

Gen.	$k = 0.01$	$k = 0.05$	$k = 0.10$	$k = 0.25$	$k = 0.50$	$k = 1$
0	0.0010000	0.0010000	0.0010000	0.001000	0.001000	0.001000
1	0.0010000	0.0010000	0.0010002	0.001001	0.001004	0.001016
5	0.0010001	0.0010011	0.0010042	0.001025	0.001092	0.001309
10	0.0010002	0.0010043	0.0010166	0.001092	0.001310	0.001915
15	0.0010004	0.0010096	0.0010315	0.001190	0.001596	0.002578
20	0.0010007	0.0010167	0.0010613	0.001310	0.001915	0.003218

decrease in 10 generations from 0.1 % to 0.0994 %. If we set one generation at 25 years, this space of time would cover 250 years. If 10 % are transferred to the upper class, the frequency of the character-bearers will, in the same time, decrease to 0.09414 %. A noticeable effect is

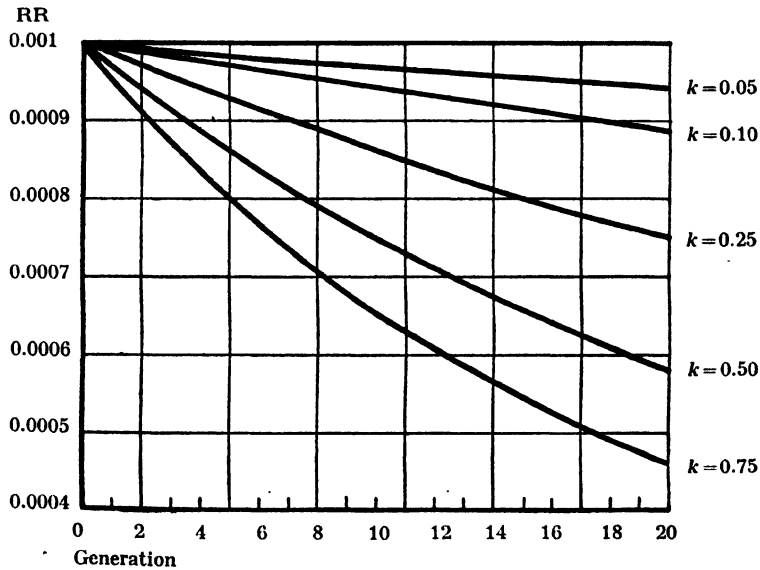


Fig. 27. Composition of the lower class in successive generations when it embraces 95 % of the population, the character-bearers at the start have the frequency 1 ‰ and the transference to the upper class has the frequency 5 % ($k = 0.05$) to 75 % ($k = 0.75$) according to formula 29. The figures are valid also for partial selection of varying strength in regard to a recessive, monohybrid character in the population.

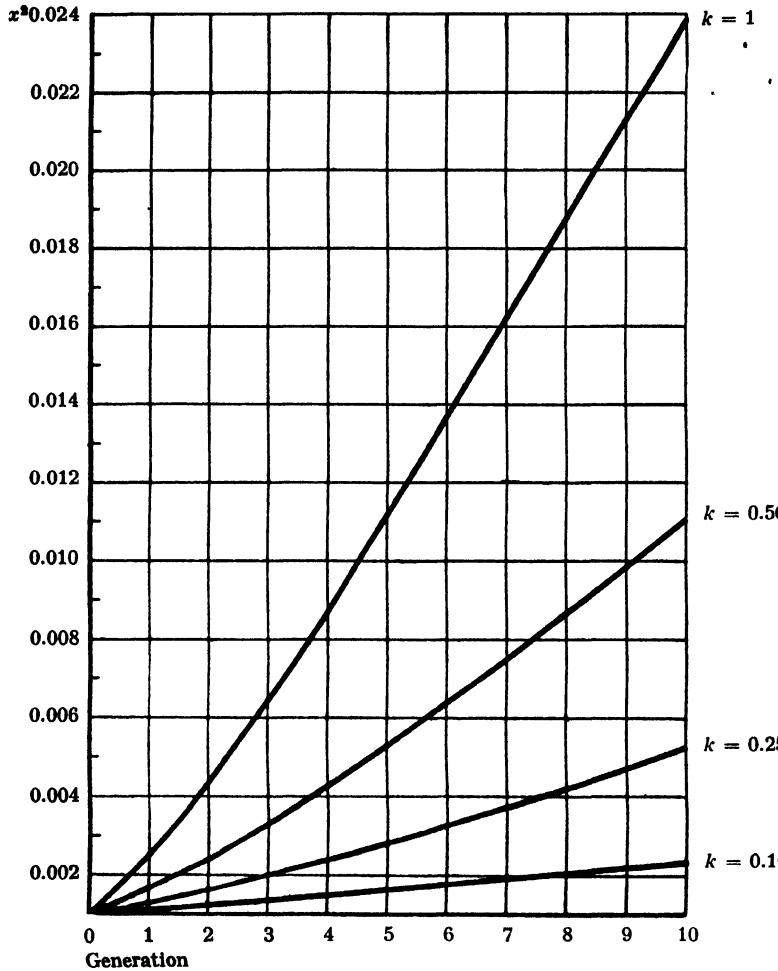


Fig. 28. Composition of the upper class in successive generations when it embraces 5% of the population and the character-bearers at the start have the frequency $1‰$ and when the transference to the upper class has the frequency 10% ($k = 0.1$) to 100% ($k = 1$) according to formula 90.

not reached until there are higher values for the selection. If half of the character-bearers are transferred, the frequency in the lower class will, after 10 generations be 0.07489%. Theoretically, it may possibly be of interest to state that if all character-bearers are transferred, the frequency sinks in 10 generations to rather more than half, namely 0.05766%.

If we look at the upper class we find that in slight selection, when only 1% of the character-bearers have worked themselves up, the frequency of the character rises to 0.1117% in 10 generations. If the selection amounts to 10%, there is a more noticeable difference: after the same time the frequency is 0.2417%. The character-bearers are, in other words, rather more than twice as numerous in the upper class as in the lower. When the intensity of selection is extremely high, the change is very pronounced. If half of the character-bearers have worked themselves up, the frequency rises in 10 generations to 1.112%, and if they all do so, to 2.389%. The figures show that a selection in respect of social standing has no or only little importance for the character-bearer frequency of the lower class, but this notwithstanding, can be thought to have a not inconsiderable effect on the constitution of the upper class.

Finally it is of interest to examine the effect of this selective transposition to isolates on the whole population. Obviously the effect must be that the frequency of character-bearers compared with panmixia increases at the same time as the heterozygotes decrease, and the stronger the selection is the greater importance must the process have. No appreciable difference is obtained with slight selection. If the selective circulation affects 1% of the character-bearers their frequency rises in 10 generations from 0.1% to 0.10002%. If the selection embraces half of the character-bearers, the effect is slight but nevertheless noticeable; the frequency rises to 0.1310% in 10 generations. In total selection the effect is so strong that the frequency of the character-bearers rises to 0.1915%, i.e. is nearly twice as high as at the beginning of the process.

Figs. 29 and 30 illustrate changes taking place in the upper and lower classes when the former constitutes at the start 5% of the population and the frequency of the character is 1%. Only a few values for the strength of selection are given.

We have no experience to support calculations referring to what really has happened and is happening. The conditions are naturally very different in different communities and during different periods of time. The characters of interest in this connexion are furthermore not monohybrid recessive, but are inherited in a more complicated way. The selection may be expected to take up such characters as intelligence, energy, artistic gifts, moral qualifications, appearance, etc. It has not yet been worked out how far and in what way characters of this kind

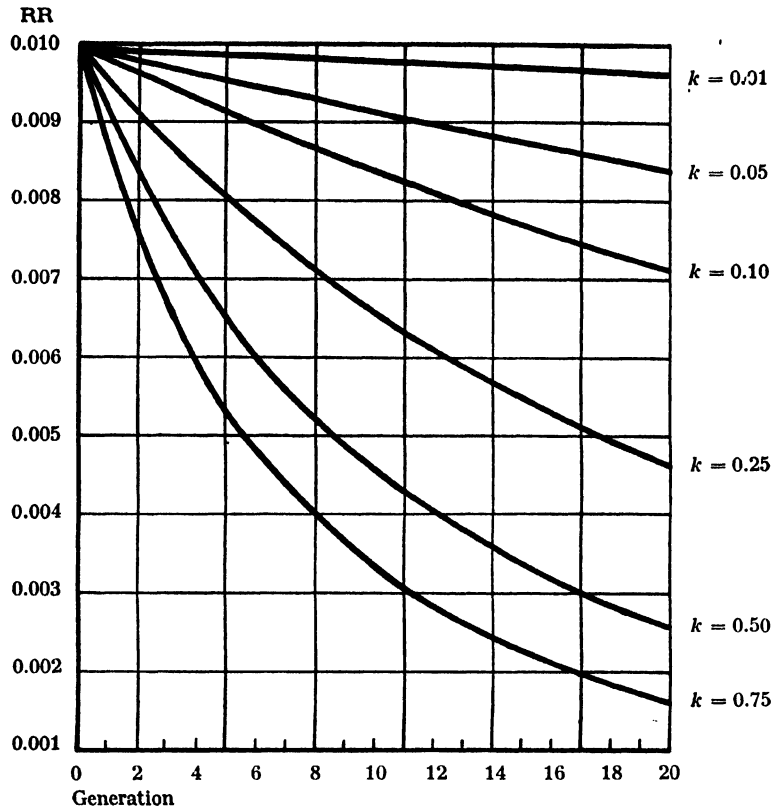


Fig. 29. Composition of the lower class in successive generations when it embraces 95 % of the population, the character-bearers at the start have the frequency 1 % and the transference to the upper class has the frequency 1 % ($k = 0.01$) to 75 % ($k = 0.75$) according to formula 29. The figures are valid also for partial selection of varying strength in regard to a recessive monohybrid character in the population.

are determined by heredity; still less is it known to what extent a circulation between the classes is present and has a selective nature. The problem has been purposely simplified here. We have contented ourselves with analysing the process only with regard to a simple monohybrid recessive character, and on the assumption that there are only two isolates, and we have furthermore arbitrarily assumed that the smaller isolate comprises 5% of the population. Thus our calculations have very little contact with what actually takes place, and it is perhaps tempting to argue that the contact is so small that the figures do not even have theoretical interest.

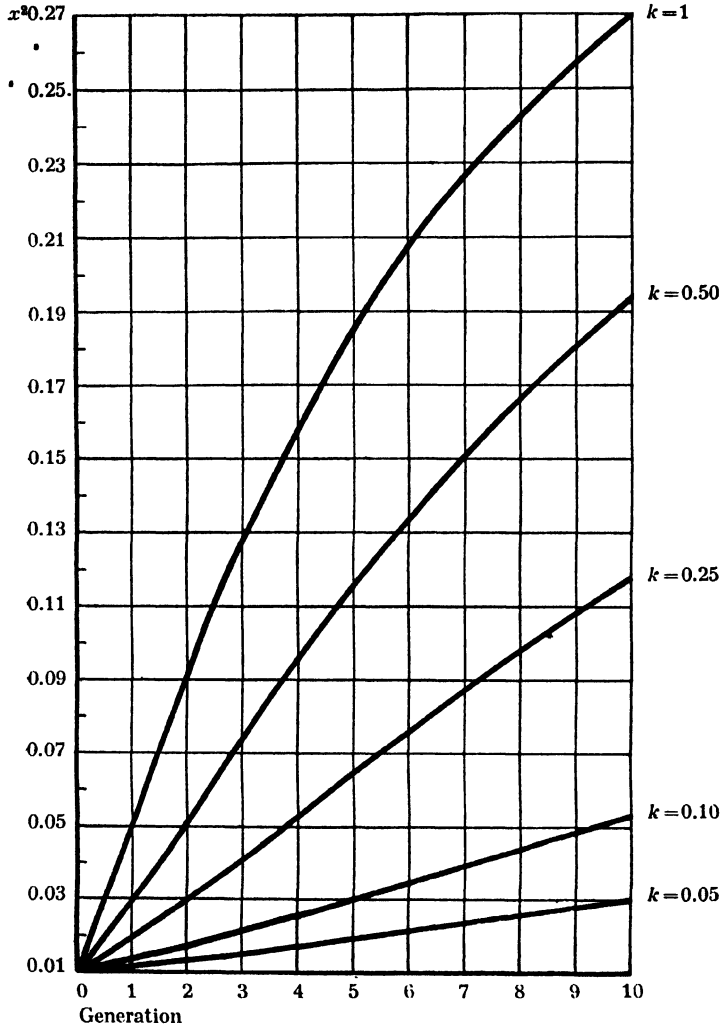


Fig. 30. Composition of the upper class in successive generations when it embraces 5% of the population and the character-bearers at the start we have the frequency 1% and when the transference to the upper class has the frequency 5% ($k = 0.05$) to 100% ($k = 1$) according to formula 90.

The aim of the calculations is, however, firstly to draw attention to the problem and indicate the lines along which it can be solved. Only if a more general interest begins to be shown in questions of this kind can we gradually obtain starting-points on which to base a rational

discussion of these questions; there is, of course, nothing to prevent mathematically developed expressions applying to characters which are inherited in a more complicated way, and a taking into account of the fact that there is more than one layer of society. Formulæ of this kind can naturally also be used for calculating the effect of the selection of importance for the constitution of the selective isolates in the bottom layer of the community. This selection would probably apply to characters to be regarded as unfavourable from a social point of view, such as poor intelligence, criminal tendencies, lack of self-control, and the like.

The other aim of the calculations is merely to demonstrate that we actually have nothing upon which to base a rational discussion of the problem. Ideas of hereditarily determined differences between the classes of society play a prominent part in current discussions of social reorganization, and in the drawing up of the Utopian schemes which play a greater or lesser part in political actions. It must assist this discussion to have it made clear that there are no criteria for definite statements, and that it is therefore important that the discussion be based on starting-points other than the assumptions of the presence or absence of marked differences in respect of heredity between different classes of the community. It may also help the discussion to have some idea of the importance a rational selection would be expected to have in a community organized in a radically different way from the one in which we live.

It may finally be of importance to make calculations based on the assumption that an ideal recruitment of the upper class has been attained from the point of view of inheritance. We imagine that an individual test is made before the individuals are given the education which is increasingly necessary in order to rise to the leading rank of a society. We further assume that the tests conducted are so reliable that no persons lacking the character rise to the upper class. We finally assume that the size of the upper class is adapted to the actual demand for a leading stratum and that a larger or smaller proportion of these special character-bearers consequently will belong to the upper class isolate. This means that in the formulæ, 87, 88, and 89 $k_2 = 0$. Under such circumstances the formula for the composition of the lower class looks as follows:

$$r^2_{a\,(n+1)} = k_1\, r^2_n. \tag{92}$$

The formula for the upper class becomes:

$$r^2_{b\,(n+1)} = \frac{(r - k_1 r_n^2)^2}{1 - k_1 r_n^2}. \qquad (93)$$

For the entire population we get the following recursion formula:

$$r^2_{n+1} = k_1 r_n^2 + \frac{(r - k_1 r_n^2)^2}{1 - k_1 r_n^2}. \qquad (94)$$

In order to reach the limiting value we can proceed as before in the case of partial assortative mating: we base our calculations firstly on panmixia and secondly on a population where the assortative mating was total, so that the heterozygotes have disappeared and only the two homozygotes are present. We then find that if the selection concerns a very rare monohybrid recessive character, having, for instance, a frequency of 0.01 %, and if $\frac{1}{4}$ of the character-bearers should belong to the upper class isolate, the frequency of the character in the population will increase somewhat and after 3–4 generations will become stable at 0.013 %. With a recessive character of somewhat commoner occurrence and having a frequency of 1 %, stability is reached after 7–8 generations if half the character-bearers belong to the upper class

TABLE 30.

Composition of the total population when it is divided up into an upper class and a lower class and when character-bearers are transferred to the upper class in different frequency and to different extent. Cf. formula 94.

Generation	$r^2 = 0.000001$		$r^2 = 0.0001$		$r^2 = 0.01$	
	$k = 0.25$	$k = 0.50$	$k = 0.25$	$k = 0.50$	$k = 0.25$	$k = 0.50$
0	0.000001000	0.000001000	0.0001000	0.0001000	0.01000	0.01000
1	0.000001250	0.000001499	0.0001245	0.0001490	0.01203	0.01407
2	0.000001312	0.000001748	0.0001305	0.0001730	0.01244	0.01574
3	0.000001327	0.000001872	0.0001320	0.0001848	0.01250	0.01642
4	0.000001331	0.000001934	0.0001323	0.0001907	0.01254	0.01671
5	0.000001332	0.000001965	0.0001324	0.0001936	0.01255	0.01682
6		0.000001981		0.0001951		0.01687
7		0.000001989		0.0001956		0.01689
8		0.000001993		0.0001959		0.01690
9		0.000001995		0.0001960		

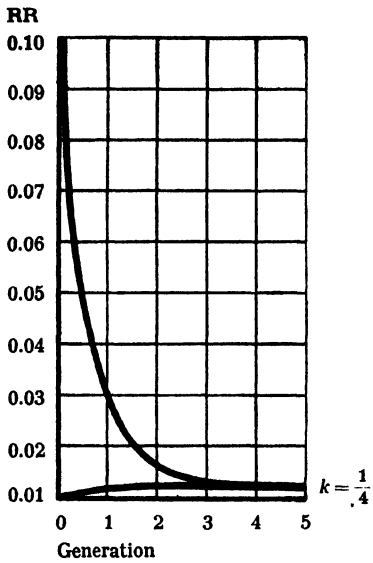


Fig. 31. Frequency of character-bearers in a population when a monohybrid, recessive character at the start has the frequency 1 % and ¼ of the character-bearers are transferred to the upper class. In the calculations we have started from panmixia and assumed that there are no heterozygotes in the population because of total assortative mating.

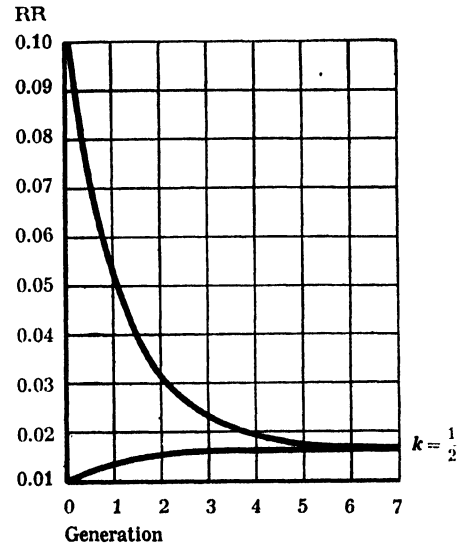


Fig. 32. Frequency of character-bearers in a population when a monohybrid, recessive character at the start has the frequency 1 % and half of the character-bearers are transferred to the upper class. In the calculations we have started from panmixia and assumed that there are no heterozygotes in the population because of total assortative mating.

isolate. The frequency of the character-bearers in the population rises from 1 % to 1.7 %. (Cf. Table 30 and Figs. 31 and 32.) For the present the calculations are of minor practical interest, but we cannot dismiss the possibility that they may have a certain importance in the future.

Summary.

General survey.

Medical genetics can be said to have, in the main, two aims. The first is to discover *theoretically* what part heredity and environment play, and to try and find out what conditions our characters psychically and physically. For genetics there exist only heredity and environment; there is no third factor. Of course, it makes no fundamental difference that the conception of probability is extensively used in genetics (*Dahlberg*, 1945). In other words, an absolute determinism is more or less consciously postulated. The aim is neither more nor less than to try to solve the problem of life in a manner as though, after acquiring exhaustive knowledge of the hereditary factors and environmental conditions governing an individual, we could "understand" the latter sufficiently to be able to fit him into his logical connection.

The other aim is of a *practical* kind. It is to discover what heredity and environment signify for individuals and populations, and above all to predict the constitution of the individuals to be born. The problem is, then, to find out under what circumstances the hereditary composition of a people is constant, and how it can be expected to change in the one direction or the other under the influence of special factors. The task is the same for individuals: namely, to obtain information making it possible to predict the constitution of the offspring from the unions between individuals (of whom as much as possible is known). From both points of view the investigation into the part hereditary factors play is naturally more interesting with regard to commoner characters than with regard to more rare ones. It must, however, also be taken into account that rare characters can, from both social and individual viewpoints, stand out as particularly significant by virtue of their nature. An individual with a hereditary constitution occasioning extremely low or extremely high powers makes more mark on society than one with so-called normal characters. For this reason, genes which occasion defects and exceptional talent respectively are of especial interest.

When we wish to assess individuals, we must of course differentiate between individual and social points of view. From the point of view of the individual himself and of those closely connected with him, his life has unlimited value in so far as it is irreplaceable; this does not, of course, prevent individuals from setting other things higher than life. Conceptions and ideas of what is right or good may result in individuals in certain situations being willing to give up their lives. Here, of course, there is a great variation not only from individual to individual but also for different populations and different periods of time.

When we wish to assess individuals from a social viewpoint, sometimes economic criteria are used. An individual is then of no value if the expenses of his upbringing and existence exactly correspond to the economic return of his work during life. He has a negative value if the expenses exceed his achievement, and a positive value if they do not. Attempts have been made to carry out economic calculations from these starting-points, which are undeniably of a certain interest. Obviously, however, the figures are of greater interest in questions of defective individuals with negative values, even if there may well be but few people in civilized countries who are willing consistently to adopt a purely economic viewpoint, and who consider other valuations of no importance. An American author *(Dublin)* has tried to express the value of a human life in money. It seems to be a widespread opinion in America that only dollars and cents can make an American act rationally, whereas nothing can induce a European to do so. As regards exceptionally gifted persons, finally, the problem is even more difficult to solve, as we have no criteria for gauging the value of their achievements from an economic point of view. The same naturally holds of persons of a more average level of intelligence who happen to have been given a leading position in a country.

It is clear that talent can be of very different types and be assessed in very different ways. Some, for example, set artistic talent highest, others straight thinking and a faculty of combination, and some consider a strong will combined with a greater or lesser degree of ruthlessness to be more valuable than anything else.

As time has gone on, a large number of investigations have been carried out within human genetics. The rediscovery of *Mendel*'s law at the turn of the century was followed by a successful attempt at showing that this law held for man also. It is easiest to show this in

respect of rare diseases, which have to a certain extent the nature of curiosities. For this reason particular interest was taken in characters of this kind. It was furthermore natural to try and copy experimental genetics, so that the investigations often tended to take the form of descriptions of families, within which several cases of a rare character occurred. The results were drawn up in the form of family trees. Starting from the first ancestors, it was found that characters appeared among the offspring in one or more generations in the way *Mendel*'s law would lead one to expect. It may be noted in passing that the method used was faulty. Those concerned did not, as in experimental genetics, begin with a given crossing and investigate the constitution of the offspring. Instead, the ancestors were selected because the constitution of the offspring was known. That is to say, the answer to the question set up was to a certain extent already given, and the analogy with the experimental investigations was in point of fact only apparent. It is therefore not always easy to evaluate the material collected. It is difficult and sometimes impossible to determine what part selection of this kind have played in investigations of this type.

Now, crossing experiments cannot be made on man; investigators have to content themselves with analysing the crossings which occur in human populations. This means that other methods must be used in human genetics than in experimental genetics. The special circumstances in man furthermore lend interest to other aspects of the question. It is desirable that, when planning investigations, some consideration should be paid to the problems indicated in this work. In other words, it is to be wished that human genetics should not follow too slavishly the same lines as experimental genetics, though it is and always will be necessary for the two trends to maintain close contact.

It is now possible theoretically and mathematically to bring out in relief the problems which are of first interest in human genetics from a population viewpoint. We then see that at present there is no empirical information for solving a number of very important problems. We lack data as to the incidence of consanguineous marriages and assortative mating. We know little about isolate boundaries and movements within populations, etc. It should, however, not be impossible to extend our knowledge on these points, having once seen clearly that such data are extremely important. The mathematical analysis of populations from a hereditary point of view may still be deficient on many

points, and the empirical background for an analysis of this kind exceedingly scanty—nevertheless there is some reason for attempting, even at this stage, to give a survey of the problems and of the results so far attained, and for a brief discussion of them based on certain initial assumptions.

For our analysis we use as starting-point that, as regards heredity, a person has six different possibilities. *Firstly*, he can marry (and propagate) at random. If marriage is contracted in this way, panmixia is said to obtain. *Secondly*, he can refrain from marrying or propagating to a greater or lesser extent than the average. If a group of character-bearers behaves in this way, we have selection. *Thirdly*, a character-bearer can contract a blood marriage. If such marriages occur to a greater extent than a chance estimate would indicate, inmarriage is said to obtain. *Fourthly*, a person may be more inclined to marry character-bearers of one certain kind than of other kinds. The most important possibility here is that character-bearers of a certain kind have a greater tendency to marry another than chance dictates. This is called assortative mating. *Fifthly*, a person who gets married has not the possibility of marrying over a whole population. His freedom of movement is limited by certain geographical and social conditions. He marries within a certain district and within a certain class, and he has small prospects of marrying outside the limits of these two. This means that a population contains isolate boundaries. *Sixthly*, we have to consider the possibility that a person getting married has offspring who deviate from what one would expect on account of mutations having taken place. These different possibilities do not, of course, exclude one another.

Thus, when selecting a marriage partner, a person may choose at random, not choose at all, choose a relation, choose within a given isolate, choose a character-bearer of a certain kind, and, finally, a mutation may enter into selection. Events of this kind may result in deviations from what is to be expected under panmixia, i.e. coming generations get a constitution differing from earlier ones. If, on the other hand, panmixia obtains, the hereditary constitution of the population is constant from generation to generation.

It is primarily of interest that selection and mutation may cause the hereditary constitution of a people to undergo a change; inmarriage, isolate effects, and assortative mating, on the other hand, do not alter the constitution, but only cause a union of genes to form homozygotes to a greater or lesser extent than is to be expected in panmixia. These

processes do not set up any change of the gene frequency in the population, and if panmixia sets in after such processes have been going on for a time, we again get, after a shorter or longer period, the composition of the population that it had before the processes started. But, if the changes set up by inmarriage, assortative mating, and isolates are reversible in theory, this does not mean that in human populations it is always possible to cancel the effect of such processes and revert to an earlier state.

Selection and *mutations*, then, alter not only the frequency of homozygotes and heterozygotes in a population: they also affect the gene frequency. Thus, if after a time the processes are thought to be cancelled and panmixia again sets in, we would get a composition of the population other than the one we had at the start. We have no exact data as to the frequency of *mutations*, but we have every reason to assume them to be very rare; this means that the changes they can be expected to set up proceed very slowly, and their effect on a population is hardly noticeable for a few generations. Mutations are therefore of no very great interest to human genetics; their primary interest is in connexion with long-term problems, e.g. when dealing with evolution in zoology and botany.

Total *selection* immediately eradicates monohybrid dominant character-bearers. In partial selection the rate of the process depends on the strength of the selection. The same is true of conditional characters, when the gene is dominant and there is total selection. In a case of this kind it is customary to speak of dominance with certain manifestation probability. Sometimes the term penetrance is used. At times, however, these terms are only used to express the fact that, owing to factors unknown, a certain gene combination occasions a certain character only in some cases. The causes may be environmental factors but may also be special genes, which are not always present but only have a certain frequency. There is reason for avoiding these terms on account of their lack of clarity. They do not give a clear idea of what the author means, and in many cases they mislead readers into thinking he knows something about the subject, whereas actually he is only justified in stating that no definite assertions can be made.

The main interest lies in monohybrid recessive characters, or such as are inherited in a more complicated manner, since serious defects early coming to the fore can be dominant only if they are extremely infre-

quent, e.g. caused by mutation. Selection has its greatest importance for recessive characters if it affects frequent ones. Then, even if it is slight, it can cause considerable results in a short time. If selection was present in earlier generations it has had its main effect and can no longer have any appreciable result. The problem is to find out the effect of selection processes of a later date.

A selection that has been active for a large number of generations should result in the reduction to a very low frequency of the characters against which it worked. In theory, we would then expect the frequency of the character to approach the state of equilibrium when the character-bearers which are eradicated by selection are balanced by mutations. We call this limit the least heterozygous limit, to emphasize that the state of balance is attended by a relatively high frequency of heterozygotes which unite at random and give rise to isolated character-bearers. These derive practically always from normal parents, who are heterozygotes. This situation should obtain for serious hereditary defects which become evident before or around puberty. In other words, particular measures such as sterilization, for example, do not avail noticeably to decrease the frequency of characters occasioning a very low fertility. Juvenile amaurotic idiocy is an example of a character which is more or less at the state of balance since, though character-bearers are extremely rare, there is a relatively large number of heterozygotes for the character in the population. Four or five of such character-bearers are born in Sweden every year; they die towards the age of puberty and never propagate—a selection more effective than sterilization. More than 50 such individuals exist in Sweden (*Sjögren*, 1931).

We might remind readers that selection against recessive characters, even if it is absolute, only makes the character's frequency tend to 0 asymptotically; this means that the character cannot be completely eradicated in finite time. To illustrate this, readers may remember that, in monohybrid recessivity, to every character-bearer who is prevented from propagation there are two heterozygotes, these last—if the gene is very rare—corresponding to the two heterozygous parents. This implies that if the population is doubled per generation, the number of heterozygotes in the population (but not their frequency) increases slightly.

It should be remembered with respect to serious hereditary defects that, since time immemorial, such character-bearers have hardly had

the possibility of propagating. When the parents died the defectives had to resort to practically non-existent charity. Social viewpoints and humane treatment have only appeared very late in the history of mankind, and even generations now living are appreciably affected by such considerations only to a very small extent. The help accorded defective individuals, even in the most civilized countries, is not of an extent to enable them to propagate freely. Earlier on they lived on the brink of want and their propagation was certainly very limited. On these points of view we may expect to find that the frequency of the hereditarily defective in different countries is not very different, and that even in populations living at a very primitive stage it is about the same as elsewhere. Unfortunately we lack reliable data making possible more exact comparisons.

If the selection is of no very great importance as regards rare hereditary defects, it should also be of no appreciable importance when applied to rare advantageous characters, such as extreme talent. We might possibly say that, during several generations, the Catholic Church applied a selection against extreme talent. In olden times gifted individuals not belonging to the upper classes, had practically speaking, only one possibility of obtaining intellectual work, and that was to become churchmen. Talent became thereby the object of selection, since on account of the celibacy rules priests were not allowed to have children. In spite of this there is no marked difference between the frequency of great talent in Catholic countries compared with other countries. If, for a longer or shorter period, the rulers of a country do not tolerate the independent thought which is an integral part of exceptional talent, and therefore try to eradicate this character, it may be of comfort to know that, though this admittedly affects the cultural level in the country, it cannot lead to a disappearance of the character, or even to an appreciable change in its frequency.

If the homozygosis in a population is altered on account of inmarriage, assortative mating, or isolate influences, the state of balance that exists between mutations and selection may be disturbed. Isolate-breaking may lessen the homozygosis, for example. This means that the least heterozygous limit gets displaced. There is then no longer a balance between mutations and selection. Even a moderate displacement of the state of balance means that it will take infinite time before equilibrium is again reached, and we can calculate that it will be more than 100 generations before a small difference is reduced

by half. The same holds if the state of balance is altered by decreased inmarriage. Lethal and sublethal genes, and also such genes as occasion serious congenital defects and the like, are then in a position to spread more, and if, for example, inmarriage is introduced afresh after some thousands of years, it might set up an increased frequency of character-bearers. This may be thought to involve a danger. It might be asserted that processes thus upsetting the state of balance between selection and mutations are unfavourable. Of course, the genes are of no consequence as long as they are latent; for this reason, we can, if we do not look far ahead, say that in each case processes setting up increased heterozygosis are an advantage. How far the momentary gain is to be considered outweighed by a very questionable future disadvantage is, at bottom, a subjective question.

Let us assume that it is possible by diminishing the heterozygosis and increasing the frequency of homozygotes to get an effective selection during the course of a few generations, and that then there automatically sets in an increased heterozygosis with a constantly lower frequency of hereditary defectives than corresponds to the state of balance prevailing earlier between selection and mutations. The answer to the questions as to whether this course should be adopted naturally depends on how far one considers generations now living should be sacrificed for future ones. Those interested in eugenics not infrequently maintain that all should be sacrificed for coming generations, whereas social behaviour is, on the whole, usually dictated by very short-term viewpoints and by the interests of those now living. There is, of course, no possibility of objectively weighing up the interests of those now living against the interests of future generations. If we assume that the interests of individuals should be accorded the same weight regardless of the time at which they live, the present generation ought to bear any burden if it can thereby win a slight advantage for coming generations. If we take it that mankind is going to live on for a considerable time, the sum of gain for the countless future generations must outweigh any disadvantages, however great they may be, for one or a few earlier generations. If, on the other hand, it is assumed that a population is going to diminish and disappear, and if all individuals are considered of equal value, it stands to reason that the burdens should in certain cases be shifted on to the smaller future generations. Actually, it is of course a matter of choice how much present generations should give up for coming ones; an objective

judgment on this point cannot be given. In point of fact the general attitude is probably that the longer difficulties can be put off, the better—not least from the point of view that there is always the hope of being able to get out of the difficulties which we cannot even glimpse at the present.

As regards the frequency a character can reach on account of a tendency to mutations, we may remember that genes arising through mutations not infrequently disappear at random. One factor determining the probability of this is the size of the family. If a gene has arisen and is present in an individual in heterozygote form, obviously the risk of the gene's not being represented in the next generation is larger in a population where the fertility rate is low than in one where it is high. Actually, we have to take into account not only that mutations disappear at random to a large extent, but also that they multiply at random. It is, of course, easier for a gene to reach a high frequency in small isolates than in large. When the isolates are small, we have to reckon with a complete absence of certain genes in some of them, and a frequency which is larger or smaller according to chance in others.

Just as there has been a tendency in some quarters to overestimate the importance of selection (above all in the form of sterilization), so has there also been a tendency to ascribe an undue effect to *inmarriage*. It should, however, be remembered that, strictly speaking, all marriages are consanguineous marriages, provided we assume uniform derivation for the races of man. If we calculate the number of ancestors for an individual on the assumption that they were not related we very soon get astronomical numbers far exceeding the number of individuals who have lived on earth. A given population with a given frequency of inmarriage cannot therefore be compared with a theoretical population where there is no inmarriage whatsoever. A suitable starting-point for a comparison is a population with panmixia, in which the blood marriages occur at random. If the population is large, the frequency of marriages between near relations will be practically 0.

An overestimation of the effect of blood marriages may perhaps be caused at least in part by the fact that repeated crossings of brothers and sisters for generation after generation in experimental genetics has given a very marked effect: the heterozygotes practically disappear after a comparatively small number of generations. In man, marriage between cousins is the most intimate blood marriage

to be reckoned with in practice. These marriages have little effect on a common character. If a character is rare, they have a not inconsiderable importance, but then, of course, the character plays but a small part in the population. If a recessive character occurs in 25 % of the population under panmixia, and if suddenly only marriages between cousins were to be contracted, then in the next generation the frequency of the character would rise to 26.56 %. If, on the other hand, a character is very rare, e.g. the gene has occurred one single time through mutation, character-bearers can only arise from blood marriages. If such marriages are very frequent and the gene very rare, it should be possible appreciably to diminish the frequency of the character by forbidding such marriages, provided that the character either is recessive or is inherited in a more complicated way. (When there is dominance, the blood marriages make for a slight diminution of the character's frequency.) However, since the population is divided up into isolates, we cannot have both high frequency of inmarriage and rare genes. There must be at least two heterozygotes in an isolate to produce a character-bearer. If the isolate is large the gene may have a low frequency, but in that case cousin marriages are scarcely usual. If the isolate is small, the frequency of cousin marriages is higher, but the gene cannot then be extremely rare. These circumstances balance the effect of the cousin marriages, so that in practice we have at most to reckon with 15–30 % of the parents of the character-bearers being cousins. This tallies with the results found when investigating rare characters. In juvenile amaurotic idiocy 15 % of the parents are cousins. In retinitis pigmentosa the corresponding figure is 17 %, in Friedreich's ataxia 9 %, in albinism 17 %, etc. Thus, a greater effect as regards rare hereditary defects would be achieved by forbidding cousin marriages than could conceivably be achieved by sterilization. All rarer recessive characters, or those inherited in a complicated way, would be simultaneously affected, and this total effect would not be very small. It would, however, only act once: for simple mendelian characters nothing would be gained in following generations.

We might fear that a prohibition of cousin marriages might also give a diminution of rare desirable characters, such as extreme talent of a certain kind, etc. Characters of this sort are probably not inherited as monohybrid characters, however, but have a more intricate mode of inheritance, so that the effect on these characters will, in

any case, be far less strong. The fact that cousin marriages have been forbidden in a number of countries is hardly due to eugenic considerations, however. The weaving of illusions which to a certain extent is a prerequisite of marriage is not so easy vis-à-vis persons who are near relations, and who are well known to one another. On this account marriage between cousins has perhaps come to appear as "contrary to nature". Not until much later does one try to rationalize one's behaviour. If we want to discuss a prohibition of cousin marriages from the point of view of eugenics, we must of course take into account that a measure of this kind implies interference in the individual's freedom to act as he likes. If we assume that the State is to accord to the members of society as great a freedom as possible, and should only intervene when there are definite reasons for so doing, the measure is disputable. In some quarters genetical "results" have been very zealously applied, which results subsequently proved illfounded. This invites caution.

The fact that inmarriage affects the frequency of all rare characters which are inherited recessively or in a more complicated way means that it causes a correlation between rare characters. If we start with rare character-bearers, we chose the offspring of cousin marriages to a particularly large extent, and we must therefore expect to find in them and their brothers and sisters a raised frequency of other rare characters. This may well in part explain why malformations of different kinds relatively often occur together, and why a marked occurrence of rare defects (e.g. deaf-mutism, retinitis pigmentosa) are found in association with other rare characters. A correlation between characters may, of course, be due to linkage but may also be due to inmarriage. We have finally to reckon with the possibility of a higher frequency for rare characters in small isolates. This makes for a correlation between the characters of a similar kind to that caused by inmarriage.

In actuality there is, as has been stated above, a connexion between isolates and inmarriage. A population is divided up into smaller parts, within which panmixia can be assumed to obtain. These *isolates* can be geographically or socially demarcated. In certain cases the boundaries are sharp, in others vague, and it may happen that there are no real limits at all. In spite of this, a given person has greater prospects of marrying persons who live at a slight or a moderate distance, and, practically speaking, no prospects of marrying persons

at a great distance. In such a case we have isolation but no sharp isolate boundaries.

We can now use the marriages between cousins to get an idea of the size of the isolates. If they are small, the frequency of such marriages is high, if large, it is low. With the help of these marriages we can calculate an idealized isolate comprising that number of individuals who, at a certain size of the family, would correspond to a given cousin-marriage frequency. We then substitute an average probability of marriage for a varying one. In various countries the frequency of cousin marriages has appreciably diminished towards the present time; this may well be linked up with industrialization, moving to the towns, and better communications. We can calculate that this corresponds to an increase of the average isolate size from 200 up to 800 individuals in a number of Western European countries.

However, we cannot assume that cousin marriages correspond under all circumstances with what is to be expected in panmixia. In countries where the parents arrange the marriages the frequency of cousin marriages should be higher than one would expect from the size of the isolates. It should further be influenced by isolate-breaking to a lesser extent than is the case in other populations, but it ought naturally not to be altogether unaffected, since the breaking of the isolate should, after all, make it less possible for the members of a family to maintain contact with one another. The relatively high frequency of cousin marriages in France may possibly be linked with social factors of this kind. Under such circumstances it is interesting to get more reliable and more varied data as to the cousin marriages in different populations.

It may finally be stated that a high cousin-marriage frequency among parents of character-bearers provides an important pointer in judging the part hereditary factors play. Far too restricted use has hitherto been made of this possibility. If, for example, a disease appears relatively often in parents and brothers and sisters of diseased persons, this may be due to environmental factors (infection). A raising of the frequency of cousin marriages can hardly be attributed to anything other than hereditary factors. In comparisons, that figure for the cousin marriages must of course be used that characterizes the isolates from which the character-bearers have been taken.

In discussing the breaking of isolates, it is to a certain extent a matter of choice whether this process is to be considered the essential

one, or whether most stress is to be put on the diminished inmarriage frequency. Even if methods for an estimation of isolate size and isolate-breaking can be obtained with the help of the cousin-marriage frequency, we have at present no other direct data for assessing the degree of isolation. It is possible we might get data to afford clues here. Needless to say, a postulate is that we adopt the view-points indicated here and, hitherto, little known within human genetics.

To clarify the relationship between isolate and blood marriages we will imagine a definite isolate, e.g. an island, on which the population rapidly grows. This means that if panmixia obtains the marriages between cousins will decrease in frequency. Notwithstanding this, the frequency of character-bearers will not be changed. This is due to the fact that more distant degrees of blood marriages increase in frequency, and this balances the decreased frequency of the cousin marriages. If we could register blood marriages of a more distant degree, it should be possible to regard the process purely from the point of view of such marriages. As, however, this is not possible, it is more appropriate to analyse the process from the point of view of the isolate. This aspect holds for a number of problems of very great import.

Now isolate boundaries are of no importance for the heterozygous frequency if the populations in the different isolates have the same constitution. On the other hand, certain genes may have a higher frequency in some isolates than in others; taking the character-bearers as starting-point we will, if we disregard the isolate boundaries, come to assume a higher proportion of heterozygotes than actually exist. In the extreme case of two isolates where the one gene is present in all individuals in one and completely lacking in the other, there are no heterozygotes, and we should then draw radically wrong conclusions if we disregarded the isolate boundaries when trying to form an idea of the gene proportion of the population.

Actually, very important differences between the isolates are to be expected for rare characters. The isolates naturally vary very greatly in size in a population. The one extreme is the large towns, the other small villages in a region of sparse population. If mutations arise in a population, they may disappear at random, because those concerned do not propagate, etc. Or they may set up by chance a moderate number of heterozygotes in later generations. If the gene is recessive, it cannot assert itself and become the object of selection before the fourth generation at earliest, since marriages between nearer

relations than cousins are very rare, and marriages between brother and sister practically never take place. The probability for a mutation to reach a moderate frequency by chance is naturally far greater in a small isolate than in a large one. For this reason rare defects are found primarily in small isolates, in remotely situated villages, where as a rule comparatively primitive conditions prevail and where marriages between cousins and other relations have a high frequency. It is not infrequently asserted that the defective individuals in the isolates and the primitive cultural conditions are a sign of degeneration due to inmarriage. This is wrong, of course. There is no reason for assuming that the hereditary constitution of the population of small isolates is either better or worse than in large isolates, apart from the specially high frequency of the gene in question. The essential factor in the process is not inmarriage; a larger population with the same gene content but lesser cousin marriages would display the same frequency of character-bearers. The important factor is the narrow isolate boundaries which are caused by the lack of communications, etc. As has been pointed out above, the improved communications, moving to the towns, and so on, have diminished the frequency of cousin marriages, which process indicates that the isolate boundaries have been broken. We can also say that the isolates have become larger through these processes. For rare characters, we can assume that if there are such in an isolate, it is hardly likely that the same gene is to be found in neighbouring isolates. The frequency of the character-bearers therefore is lowered by crossings over the isolate boundaries. The genes become dispersed in heterozygous form. In the extreme case this process goes on in proportion to the increase of the isolate. As has already been mentioned, the frequency of cousin marriages can be used to calculate that the isolates in a number of Western European countries have been doubled at least, and possibly trebled; this should have made for a very appreciable decrease of the frequency of rare defects without consequent decrease of the frequency of the genes corresponding to the defects. This must imply an advantage, since the process is irreversible. If most stress is put on the diminished blood marriages in this process, the situation is wrongly assessed if only the marriages between close relations are taken into account. The frequency of character-bearers has probably diminished far more than what the diminution of the cousin marriages can have caused. If for some reason the frequency of the cousin marriages should in the future increase,

this should not increase the frequency of character-bearers up to the ealier level.

Meanwhile, the official statistics do not show the decrease of defectives these paths of thought lead us to expect. It must be remembered that the registration of such defectives has become more and more complete, however, though it is still far from satisfactory. Sweden is thought to have relatively reliable population statistics. In spite of this, the frequency of epileptics, for example, at the last census in 1940 amounted to only 4349. Data as to defects are not as a rule willingly given to authorities. There is, however, one exception to this, namely the examinations of conscripts. On data from these it can be calculated that the number of epileptics in Sweden should be about 12 000; this means that there is plenty of room for an increased frequency through improved registration, even if the actual frequency of hereditary epilepsy were to decrease appreciably.

As the isolates are smaller in the countryside than in the towns, we ought to expect a higher frequency of hereditary defects among the country population than among that of the town. The difference should, however, in part be due to the fact that a selection takes place at the migration into the towns. The defective remain behind in the country to a comparatively great extent. As, however, individuals with recessive defects practically exclusively derive from parents who are heterozygotes, these circumstances ought only to have effect in the last immigrated generation. The heterozygotes should be as numerous as in the original population.

Concerning this it may be interesting to compare figures from country and town and from different regions in Sweden. The figures are taken from the census of 1930. Cf. Table 31.

When interpreting these figures we must remember that only a certain number of these defects are conditioned by heredity. At present we have no possibility of judging definitely in each separate case whether the defects are conditioned by environment or not. It may further be stated that the headings used cover a number of different hereditary defects, blindness, dullness of intellect, lameness, etc. They are composed, that is to say, partly of a number of defects conditioned by genes, partly of defects due to environment. Finally, as has already been said, the registration is incomplete. In these circumstances we must be content with saying that frequency differences are found which, on the whole, correspond to what we would expect from the size of the

TABLE 31.

Frequency of defective individuals in per mille in different administrative areas in Sweden according to the census in 1930.

Administrative area	Blind	Deaf-mutes	Feeble-minded	Insanes	Epilep-tics	Cripples
Town of Stockholm	0.86	0.49	1.23	3.93	0.37	8.57
County of Stockholm	0.67	0.74	2.69	3.66	0.65	10.99
» » Uppsala	0.98	0.99	3.17	4.90	0.82	11.81
» » Södermanland ..	0.86	0.73	2.91	4.32	0.83	11.41
» » Malmöhus	0.49	0.69	2.28	4.44	0.71	9.20
» » Västerbotten	1.52	1.45	3.62	4.47	0.77	11.71
» » Norrbotten	1.32	1.15	3.26	4.53	0.99	11.36
Towns of Sweden	0.73	0.74	1.62	4.51	0.50	9.51
Rural parishes of Sweden .	1.10	0.93	3.46	4.54	0.81	11.68
The whole of Sweden	0.98	0.87	2.86	4.53	0.71	10.97

isolates. The frequency of defectives is lower in towns than in the country, is extremely low in Stockholm and extremely high in the most northerly parts of the country (Västerbotten, Norrbotten), where the isolates are comparatively small. (The absence of noteworthy differences as regards the frequency of the insane is probably connected with the fact that they are taken care of and registered to a far greater extent in the towns than in the country.) It should in any case be interesting to try and analyse the figures for the frequency of the defectives in the different districts from the standpoint used here.

Summing up, we may say with regard to rare defects that sterilization can hardly be thought to affect their frequency to any extent worth mentioning. More effect would result from forbidding cousin marriages. The process which is of the greatest importance is isolate-breaking. In some quarters it has been contended in the field of eugenics that the peasant population is the nucleus of the people, and partly on this ground steps have been taken to try to prevent them moving into towns and to keep them in the country. If we think here of the frequency of defects, this view is wrong. The defects have a higher frequency in the relatively small isolates of the countryside, and if we want to diminish their frequency we should encourage moving to the towns.

Now, the frequency of the defectives is by no means of crucial importance for a population, however. Even if a comfortable existence were made available for them, the cost would be negligible compared with the enormous extravagance of the outlay that the organized mass mur-

ders due to war involve. Far more important, of course, are the sufferings that the defects bring with them for the character-bearers and their parents.

There is talk within the field of eugenics of the frequency of the defectives, as though this had tremendous significance for the general efficiency. In point of fact the general average intellectual level and the frequency of exceptionally gifted persons mean far more for a society. As has been said above, selection has no great importance for the frequency of exceptional talent, provided it is so demarcated as to be a rare character. Whatever we may take exceptional talent to imply, it should, further, be possible to assume that a greater or lesser frequency of inmarriage plays no appreciable part in the frequency of the character, if we think of cousin marriages and similar degrees of marriage between close relations. This is because the character, in so far as it is conditioned by heredity, is undoubtedly caused by a number of genes which must meet. For such characters a higher or lower frequency of cousin marriages is of little importance. On the other hand, it is possible that isolate boundaries are of considerable importance for them. To illustrate this we will briefly discuss the importance of the isolate-breaking for stature. From the point of view of heredity there are important similarities between talent and stature. The stature in a population has a fairly normal distribution with low frequency of extremely tall and extremely short persons, and a high frequency of those of medium height. A similar distribution has been obtained from the carrying out of so-called intelligence tests. A small number of extremely short individuals are found below the range of variation of the normal distribution. This is due in a number of cases to environmental injuries, in others to special genes (dwarves, kyphosis due to tuberculosis, etc.). Analogous with this, we find, below the stupidity which is the lower limit of normal talent, a small number of individuals who are markedly defective either on account of environmental injuries (as haemorrhages at delivery) or of special genes.

It has been possible in several countries to establish that in recent years stature has increased. In Sweden the increase amounts to 9 cm in exactly 100 years. The supposition most readily presenting itself is that this is due to a raised standard of living. Actually, however, the increase in stature does not run parallel to the raising of the standard of living. There is reason to suppose that better nutrition affects the rate at which young persons grow up to about puberty. After

that, growth proceeds more slowly with good nutrition, so that there is probably no difference worth the name in adults. It has been possible to show that from 1883–1938/39 the difference in stature for 15-year-olds in Sweden is about 15 cm; for adults, on the other hand, not quite 5 cm. If the stature is determined by a number of genes which are mainly dominant, it is possible that the isolate-breaking which has taken place in Sweden and which has set up an increased heterozygosis is the essential cause of increased bodily length in adults. The author has discussed these problems in several papers (cf. *Dahlberg*, 1931 and 1938; *Broman*, *Dahlberg* and *Lichtenstein*, 1942).

As regards stature, then, the breaking of isolates would make for a decrease in the number of extremely short persons, a rise in the number of mediumly tall ones, and an increase of the extremely tall. If a similar process has been at work for intellectual gifts we should expect the breaking of isolates to have set up a decrease of the frequency of the extremely stupid, a higher mean intelligence, and an increase of extremely gifted persons.

To work out in more detail the importance of isolate-breaking for normal intelligence we need investigations into how poor abilities are inherited. If we find they are primarily inherited as a complicated recessive character, we have reason to suppose that isolate-breaking is socially advantageous, and a danger if the reverse is the case. This side of the matter is perhaps more important than the effect the isolate-breaking has had and has on the frequency of the hereditarily defective.

Seen theoretically, there is of course the possibility that the process is of no consequence and that recessive and dominant genes balance each other in such a way that isolate-breaking has no effect.

In so far as isolate-breaking affects the hereditary characters in a population, we would expect differences between town and country populations. Heterozygosis is greater in a town population. Processes of this kind may, furthermore, make for differences between different countries. It stands to reason that heterozygosis is less in a country where the inhabitants are of old standing than in one where there has been immigration and where settlement of colonization type is found. On this point there should, for example, be a difference between not only Europe and America but also between North America and England.

Thus, questions bearing on the breaking of isolates should assume an important place within genetics, and it is in the first place important to obtain primary data as to the extent of the process in different countries.

As regards *assortative mating*, too, we lack primary data upon which an analysis of the importance of such processes could be based. It has been possible to show mathematically that assortative mating very rapidly leads to a state of balance. It is therefore first and foremost of interest to investigate the extent to which processes of this kind have arisen in more recent times. They have been given greater scope by increased communications. Assortative mating can hardly play any very great part in rare characters, since the bearers, precisely on account of their rarity, have no very extensive possibilities of meeting. Isolate-breaking has, however, increased the possibilities of such a process. The extent to which assortative mating exists for ordinary characters has been very little gone into hitherto. Nevertheless we know that there is such a tendency as regards stature. Tall persons and short persons respectively marry each other somewhat more than a random estimate would lead one to expect.

In theory it is possible that there is negative assortative mating for certain characters. It is above all likely that certain afflictions making for helplessness have a curbing effect on marriages between persons with the same character. Some genes affecting the appearance of a person might give rise to negative assortative mating. Possibly there is such a process going on for individuals with strabismus. Processes of this kind should cause a slight increase of heterozygosis, but it is unlikely that such processes would have a noticeable effect in human populations.

There is reason to assume that the genotypically deaf-mutes are about half of the total number of deaf-mutes. Some of them marry outside the isolate and other inside the isolate, which is constituted through special societies for deaf-mutes and other organizations. Of course the situation also depends on the density of the population and is quite different in different countries. At present it is not possible to make exact calculations, but it should hardly be difficult to obtain information on which such calculations could be based.

We may suspect similar processes to exist as regards genes which condition special interests. For example, musical persons are brought together to a certain extent in special societies and circles, and we might with some justification speak of selective isolates. At the same time we must also take into account that the interest in music sets up direct assortative mating even in those communities where musical isolates hardly exist. No investigations on the matters discussed here have been carried out.

If there is a tendency to assortative mating as regards rare characters, e.g. hereditary defects or exceptional talent, there is reason to suppose that the breaking of isolates would cause it to play a somewhat larger rôle nowadays than has earlier been the case. The increase in size of the isolates has given rare character-bearers a greater chance to meet. The process sets up an increase of homozygosis and a decrease of heterozygosis; it thus counteracts the breaking of the isolate and the decrease of inmarriage. It is not possible to determine the effect of these processes exactly, but it seems hardly probable that the increase of assortative mating plays a very important part. Empirical investigations into this problem are desirable, however. The circumstances are naturally different with different characters. For deaf-mutes, for example, we have reason to suppose that general isolate-breaking (movement into towns) increases their possibilities of meeting. The fact that they have at the same time been given an improved training, increasing their possibilities of contact with normal persons, may well mean that the tendency to assortative mating is simultaneously counteracted. The result of these processes can only be established by empirical investigations.

The form of assortative mating which is conditioned by a special genetically determined trend of interests leads on to the question of the importance of the social class limits from the point of view of heredity. Persons who are born into the one social class or the other and who possess average characters remain, for the most part, within their class. There is, however, a certain class circulation, which implies both a moving about of persons with more average characters, and also a selective move. Persons with characters giving rise to special social effectivity have certain prospects of getting into a higher layer of society. Particularly backward persons sink down into a lower one. Here, too, we can, of course, talk of isolates with a selective moving about, but we can also put the stress on a special, possibly hereditary trend of the interests, and consider there to be assortative mating over the isolate boundaries. We have perhaps most reason to stress the latter in questions of women, and the former in questions of men. When women marry into the upper class it is possible that there is positive assortative mating as regards intelligence, but perhaps above all a negative assortative mating as regards appearance. When men work their way up into the upper classes, they have often had time to contract a marriage before they succeeded in breaking through the

isolate boundaries, and the women thus added to the upper-class isolates have the average constitution of lower-class isolates—provided assortative mating does not obtain for the group of men working their way up.

A special directing of interests is, of course, essential for the men who reach the upper classes; unless their will was concentrated on this goal, they would hardly pass the boundaries. The question then is, how far special hereditary characters are of importance. Factors of chance naturally play a not insignificant part. Other things being equal, however, exceptional talent should be an advantage, but also a strong will, a certain egocentricity, and lack of consideration for others are also great helps. It is possible that those who work themselves up are to a certain extent a selection of persons with desirable intellectual and undesirable moral characters.

It is possible mathematically to calculate the effect of the selective or assortative isolate formation implied in the boundaries of the social classes. If the character and size of the process is known, it is possible mathematically to calculate the effect of the selective or assortative isolate formation implied in the boundaries of the social classes. A selection in respect of special hereditary characters can be shown to make of necessity for a progressive effect on the constitution of the upper-class isolates. Our present knowledge is not enough to determine whether the effect is large enough to play any significant rôle, however. As the upper class is relatively small and the class circulation likewise, we can nevertheless state that the masses do not change character as a result of possible selection. For the lower classes we can assume that the question is one of a selection that is too small to have any importance worth mentioning.

It is interesting in this connexion to remember that the population in certain regions has been recruited primarily from emigrants from the lower classes in Europe, e.g. Australia and U.S.A., without any noticeable decline in quality being involved.

The problem of the character of the upper class is, of course, very difficult to solve; in any case it must be treated quantitatively on the lines indicated here. Undoubtedly there is a trend making for a difference but this trend may be too weak to be of any importance. The questions in this sphere are of very great importance. The idea that social classes arise by chance has more or less definitely been behind the demands of reforms aiming at equality. On the other hand, it has also been asserted that there are important hereditary differences

between classes of society, and that the upper layers constitute a selection with better gifts and character than do the lower. This selection, which took place during earlier generations, has established so great a difference that the upper classes can look upon themselves as an élite, which on account of the inherited quality has a special right to a more advantageous position. For this reason measures aiming to level out class differences are opposed, and it is not desired that differences in quality should be taken into consideration by further selection. From the point of view of heredity our first desire would be that the isolate constituted by the ruling classes should be constantly renewed, by a deliberate selection, analogous to the way in which defect-isolates are formed for the deaf-mutes.

In certain quarters attempts have even been made from a genetical point of view to encourage a direct resistance to class circulation—an extremely conservative view being subscribed to. In so doing it has been assumed that the upper classes have a lower fertility rate than the masses. The admission of the gifted into the upper classes exposes them to selection since they then participate in the limited fertility habits distinguishing these classes. It is, therefore, considered to be in the interest of society to retain the gifted in the lower classes indefinitely. (No time is given when society is to use their gifts.) At the same time it is asserted that the low fertility habits in the upper classes indicates a moral inferiority and an antisocial egocentricity. Greater fertility is desired among these antisocial beings.

We have indicated from the point of view of genetics a number of problems touching on the formation of social classes, partly to show that the complicated questions in this sphere are far from solved and are difficult to expound, partly also to emphasize that our present knowledge does not enable us to pronounce on the hereditary dissimilarities which may exist between the classes. The problem is very intricate, and our knowledge is so sketchy that it is not possible to express an opinion on social organization in relation to the absence or presence of special hereditary differences between different social layers. For the sake of completeness it must finally be stated that the problems naturally cannot be seen exclusively from the point of view of heredity. Organisational and economic aspects, and others, must also be taken into account.

Another complex of questions also bearing on assortative mating and isolate boundaries is that of racial differences. In most cases a race can

be defined as a group of isolates which are demarcated regionally and which exhibit hereditary differences from other isolates. When ideas as to the excellence of one's own race and the inferiority of others enter in, however, assortative mating not infrequently comes into being also. Thus the Jews, for example, have to a certain extent constituted regionally limited isolates. But they have also constituted social isolates, and we can if we like assert that there has been assortative mating in that Jews have married Jews more often than they have married non-Jewish individuals, and vice versa. In the same way the contrast between whites and negroes in America has resulted in isolate boundaries, which can to a certain extent be said to indicate assortative mating.

Racial research has, since olden times, worked with old-fashioned ideas as to genetics. The theory, accepted before Mendel, of the hereditary mass as a substance diluted to varying degrees through crossings is at the back of a number of the views advanced on races. Pure races of homogeneous constitution are assumed in the same way as, in chemistry, one speaks of pure substances. Essential differences between races are assumed by the side of the unimportant differences of appearance that can be established objectively. Mendelism has not yet thoroughly penetrated into racial research.

From the point of view of Mendelism a race consists of individuals who are of extremely varying constitution and who are homo- or heterozygotes for different genes. The variation is so great that, apart from monozygotic twins, the possibility of two individuals completely resembling one another hereditarily can be ruled out.

When investigating questions of race, the very first thing to do is to find out whether there are differences between groups of isolates within a population. One way of doing this is to see whether there is a correlation between characters. If there is no such correlation between characters inherited independently of one another, there is no reason to speak of racial differences. If there is correlation, an attempt must be made to gauge the extent of the differences present.

The ideal is to reach frequency figures for those genes which have a different frequency within the two race groups. This is only possible in exceptional cases, for example in the frequency of defects inherited in a known way. But even though an exhaustive analysis of racial differences is impossible, we can still try and get a more or less satisfactory measure of possible differences in characters whose manner of inheritance

has not been worked out. (There must, however, be good grounds for assuming that the characters are hereditary.) The most reasonable thing would seem to be to try and assess the differences in respect of the variability existing. Obviously the differences are not very important if a large part of the range of variation distinguishing the two groups compared is common. This work describes a method of gauging racial differences, the principle of which is that we investigate in the first place the range of variation for the different characters in the groups to be compared. We then imagine we mix the two groups, after which we try and separate the individuals with the help of the knowledge gained about them. The best result obtainable is when all individuals can be sorted out correctly. If the differences are small, we get a larger or smaller remainder group, which cannot with certainty be relegated to either of the two primary ones. The size of this group gives a measure of the race difference.

The method can, of course, be used to establish the extent of differences between materials, even in questions of other characters than racial differences.

The method is of special value as regards more disputable racial divisions, that is to say, when the differences are small. An advantage of this method is that we are forced to build on the knowledge we actually possess of the racial groups in question, and are unable to use more indefinite and consequently doubtful "observations"; at the same time we use to the full the exact knowledge we have. Race investigations carried out hitherto are, in many cases, much too patchy to allow of an analysis according to the method given here. When this method is used, however, it should be able to help towards giving racial research a more objective character, and combat the antiquated superstition that at present is in some quarters entitled scientific racial research.

In the previous pages we have indicated a number of applications of mathematical theory, presented in this work, for populations from a hereditary aspect. Our aim has been to try and awaken interest in problems of this kind, and in so doing to influence the trend of scientific work in this sphere. It should not be necessary to emphasize that in the general presentation given here it has only been possible to indicate the problems, and that the author has therefore chosen to dwell especially on problems with which he himself has worked.

Finally, it may be stated that the mathematical analysis of populations in respect of heredity shows that a number of conclusions hitherto

thought possible with the help of analogies from the plant and animal world have been wrong, and that therefore certain suggestions as to social measures have been ill-founded. With regard to this there may well be reason for caution in using the consequences of the mathematical population analysis also. The results that have been obtained should not be considered as definitely established before they have been empirically verified. Only then can they justifiably be used as starting-points for a discussion of practical measures.

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